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EDITORIAL

WE are happy to announce that from this issue the Journal will revert to quarterly publication.

It has been the editorial policy to publish high standard articles of clinical and scientific interest to anæsthetists. We are glad to be able to include in this issue two papers from those primarily interested in the basic sciences, and we hope that this liaison will continue. Anæsthetists certainly are unlikely to be familiar with a number of the technical terms which are used by Dr. Howarth in his paper on "Radioactive Isotopes." This is pioneer work. As this new technique is likely to become increasingly applied to medicine it will certainly repay close study on the part of the anæsthetists, as well as other clinicians, and we welcome this chance of giving our readers an early opportunity of becoming acquainted with this new method of investigation and the language which it employs.

We are also continuing our series of short biographies of great anæsthetists. The representative in this number is Dr. Gilbert Brown of Adelaide. Dr. Geoffrey Kaye has given us a fascinating study of him. Dr. Brown was the founder of the Australian Society of Anæsthetists, to which so many British anæsthetists are feeling extremely grateful by virtue of the large number of food parcels which they have received. Dr. Brown's very close connections with Merseyside will be a source of pride to our colleagues in that area. It would appear that in Australia anæsthetists have had to fight the same uphill

battle for recognition as they have fought in this country. They are assured of our good wishes and encouragement.

A new feature of the Journal will be space allotted to the publication of hints and small pieces of apparatus which may be of practical interest to anæsthetists. We have called this feature "Notes and Comments" for lack of a better name, although we had a sneaking desire for "Gadget Corner". It was realized, however, that such a title was perhaps a little undignified and would in any case limit the scope of the section. We trust that those readers, who have ideas which they have felt perhaps unworthy of publication as a large feature, will not hesitate to send them along. We would also be glad to receive reports of interesting cases which might subsequently provoke discussion.

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Readers may be interested to hear the results of the recent Diploma in Anæsthetics examination. Out of 104 candidates who took Part I, 23 were successful, and out of 95 taking Part II, 50 obtained their Diploma. Twelve successful candidates from Part I proceeded to take Part II and 8 of these were successful. This examination, of a higher standard than the old Diploma examination, is, contrary to the expectations of many, proving a great success. It is, we believe, giving rise to a type of anæsthetist who is not just a technician, but who has a good all-round knowledge of the subject and a firm grounding in the basic sciences. These young men and women are becoming respected by their colleagues in other branches of medicine, and the prestige of the examination and of the Diploma has never been higher.

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Our congratulations must be offered to Dr. Geoffrey Organe, who represented British anæsthetists recently at the Latin-American Congress of Anæsthetists in Buenos Aires, and to Dr. Soares, of Lisbon, an old friend to many in this country,

who represented Portugal. Our felicitations also, and good wishes, to Dr. Bernard Johnson, who has been asked by the British Council to lecture on Anæsthesia in the South of France.

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We understand that there is a vacancy for an experienced anæsthetist who would be willing to work at the Vellore Christian Medical Hospital in India. Medical missionary work is a vocation, and doctors in this field have a long record of distinguished service and self-sacrifice. If there is any anæsthetist who would be interested in embarking on such a career the Editors would be very glad to give further details.

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The charitable prayers of our readers are requested for those of their colleagues who have been condemned to languish in the limbo of the S.H.M.O. status, that they may be soon restored to the glory and beatitude of full Consultant status.

RADIOACTIVE ISOTOPES AND THEIR APPLICATION TO A PROBLEM IN ANÆSTHESIA

By Frank Howarth, M.D., D.P.M.

IN 1934 Joliot and Curie described the phenomenon of artificially induced radioactivity and a versatile and potent weapon passed into the hands of the biologist. With the aid of the radioactive tracer technique it is possible to estimate substances in amounts so minute as to be beyond the powers of ordinary chemical analysis, while an element in a biological system can now be assayed in the presence of excess of its chemically identical isotope. There are many other uses of the radioactive isotope but in this article it is proposed to describe briefly certain aspects of the assay of radioactive substances with special reference to a particular problem, so that those engaged in other fields can appreciate the general plan of a simple 'tracer' experiment. It is not the author's intention to compile a comprehensive bibliography of the research on this subject; such information can be obtained from the various textbooks now available such as Kamen (1947), Hevesy (1948), Lawrence and Hamilton (1948).

What is an Isotope?

An atom consists essentially of a nucleus and a number of negatively charged orbital electrons. The number of electrons determines the chemical characteristics of any particular element. The nucleus contains protons and neutrons which are each of approximate mass 1.66×10^{-24} g., the main difference between them being that while the former bears a single positive charge the latter is uncharged. An atom, however, is an electrically neutral body, hence there are as many electrons as there

are protons. It follows that, if neutrons are added to a nucleus, the nuclear mass will rise, but the nuclear charge, the number of orbital electrons dependent upon it, and hence the chemical identity of the atom, will remain unchanged. Such atoms varying in mass but not in chemistry are termed isotopes. Isotopes may be stable or unstable (radioactive) and, though the former will be of great importance in future assay procedures, having certain advantages over the radioactive forms, only the latter will be considered here. The uranium pile is a neutron generator, and when a specimen of an element in suitable form is placed within, it is often possible to add a neutron to the nuclei of the atoms. Thus stable bromine may be changed to radioactive bromine;

$$_{35}Br^{79} + {}_{0}n^{1} - {}_{35}Br^{80}.$$

This is a commonly used system of nomenclature; the superscript indicates the total number of nuclear particles in the nucleus and is usually indicated by A. The subscript, Z, indicates the number of protons (hence the number of electrons). Then A—Z indicates the number of neutrons in the nucleus.

It is not always necessary to add neutrons to an atom to prepare an isotope. It is possible to add protons, though this must always involve a change in the chemical nature of the element bombarded. Protons may be added by the bombardment of a specimen of the appropriate element with charged particles accelerated to very high velocities. The cyclotron is one of the machines designed to effect this acceleration. The charged particles may be hydrogen nuclei (protons), heavy hydrogen nuclei (deuterons: neutron + proton) or helium nuclei (α-particles: 2 neutrons + 2 protons). Thus in the classic experiment of Joliot and Curie (1934) boron was converted to radioactive nitrogen by bombardment with α-particles;

$$_{5}B^{10} + {}_{2}He^{4} \rightarrow {}_{7}N^{13} + {}_{0}n^{1}.$$

It does not follow that all charged particle bombardments

change the chemical nature of the bombarded element. Thus radioactive ${}_8C^{14}$ can be prepared from stable ${}_6C^{13}$ by exposing the latter to a stream of accelerated deuterons, during which reaction a proton is lost and ${}_6C^{13}$ gains a neutron. There are many other types of nuclear reaction but a discussion of these is beyond the scope of this article.

Radioactivity

A stable atom requires a certain combination of neutrons and protons and when there is excess of one or the other the atom tends to be unstable and it endeavours to regain stability by an interconversion of neutrons and protons. As a result of this readjustment electrons or positrons and gamma radiations are emitted and the element is said to be radioactive.

Consider radiophosphorus ${}_{15}P^{32}$. Tables show that an element already exists with 32 particles in its nucleus, i.e. ${}_{16}S^{32}$ and the unstable phosphorus tends to become stable sulphur. But S^{32} has sixteen protons while P^{32} has only 15, so P^{32} changes one of its neutrons into a proton by liberating a negative electron in the form of a beta particle.

Sometimes an electron may bear a positive charge (positron) thus ${}_7N^{13} \rightarrow {}_6C^{13}$ by the conversion of a proton into a neutron and the liberation of a positive charge. The positron has but a brief existence, however, combining almost at once with a negative electron in any material through which it has to pass. These bodies of opposite and equal charge annihilate each other and two gamma rays appear in their stead.

A radioactive isotope takes time to change from an unstable to a stable state, and the time taken for the amount of radiation from such an isotope to fall to half a pre-determined value is known as its half-life. Half-lives vary from some 10^4 years in the case of C^{14} to a fraction of a second as in Li^8.

The products of radioactive decay possess kinetic energy usually expressed in terms of the electron volt, which is defined as the energy acquired by an electron falling through a potential difference of one international volt. Thus Br^{82} has a half-

life of 34 hours, and emits electrons of 0.465 M.E.V., each associated with three gamma rays of 0.547, 0.787 and 1.35 M.E.V. (M.E.V.= million electron volts).

The degree of radioactivity of a specimen of isotope depends on many factors, and there are techniques whereby certain radioactive isotopes may be concentrated. The unit of activity usually employed is the curie and its submultiples, the millicurie and microcurie. "Curie" is a term borrowed from radium practice and is that quantity of radon (radium emanation) which is in radioactive equilibrium with one g. of radium. The millicurie is one thousandth of this and is that amount of radium providing 3.7×10^7 disintegrating atoms per second. This is satisfactory for radium whose disintegration scheme has been extensively studied, but the absolute distintegration rate of any isotope is difficult to ascertain and requires knowledge of the precise manner in which it decays. This informaton is available for comparatively few isotopes. The above figure does not necessarily mean 3.7×10^7 electrons emitted per second, since one disintegrating nucleus may be associated with more than one electron. Moreover the apparent rate of emission depends considerably upon the type of detector used, especially in the case of gamma rays. The millicurie unit has therefore many serious shortcomings. The unit difficulty does not arise in ordinary radioassay, since the investigator sets up his own standards on his particular instruments. There are other units associated with radiation measurements and for a description of these see Evans (1947).

Specific Activity

This is defined as the radioactivity per unit mass.

Assay of Radioactive Isotopes

When a charged particle passes through a gas it produces a number of ion pairs, each pair consisting of an electron and a positively charged residue derived from the atoms of the gas concerned; to this phenomenon the term ionisation is given and is the fundamental fact upon which stands most of the

techniques for radioassay. The number of ion pairs produced in unit distance by any such particle depends directly upon its charge and indirectly upon its velocity; from this it follows that gamma rays, which have no charge, can only produce ionisation by the charged particles they release during their passage. Consequently the assay of gamma radiating isotopes is not as efficient as the radioassay of beta radiating isotopes.

If two electrodes at a large potential difference are introduced into a gas through which are passing charged particles, the positive ions travel towards the cathode and the electrons towards the anode, and a current will pass through any suitable circuit of which they are a part. Such a device is termed an ionisation chamber and is the basis upon which most instruments for radioassay are constructed. Of these instruments those most widely used are modifications of the Geiger-Muller counter. Figure 1 shows two typical examples.

As stated, a charged particle passing through the gas space in a G.M. counter produces a current flow and the problem of radioassay is to detect the electrical impulse produced by each charged particle, a task rendered easier by the fact that each ion by further interactions produces more ions, thus initiating a current of detectable size. With the small tubes in common use in biology it is often necessary to amplify this current still further. Although in theory these discharges could be detected by clicks in head-phones or neon bulb flashes, etc., it is more convenient to record them with an electro-magnetically activated cyclometer or its equivalent. Since the "pulses" produced by a G.M. tube can be so rapid as to be beyond the scope of such an instrument it is usual to feed them into a scaling unit whereby a fixed proportion of the electrical pulses is fed to the recorder.

Corrections in Assay Procedures

There are a number of corrections which must be applied to an apparent counting rate determined for any radioactive sample.

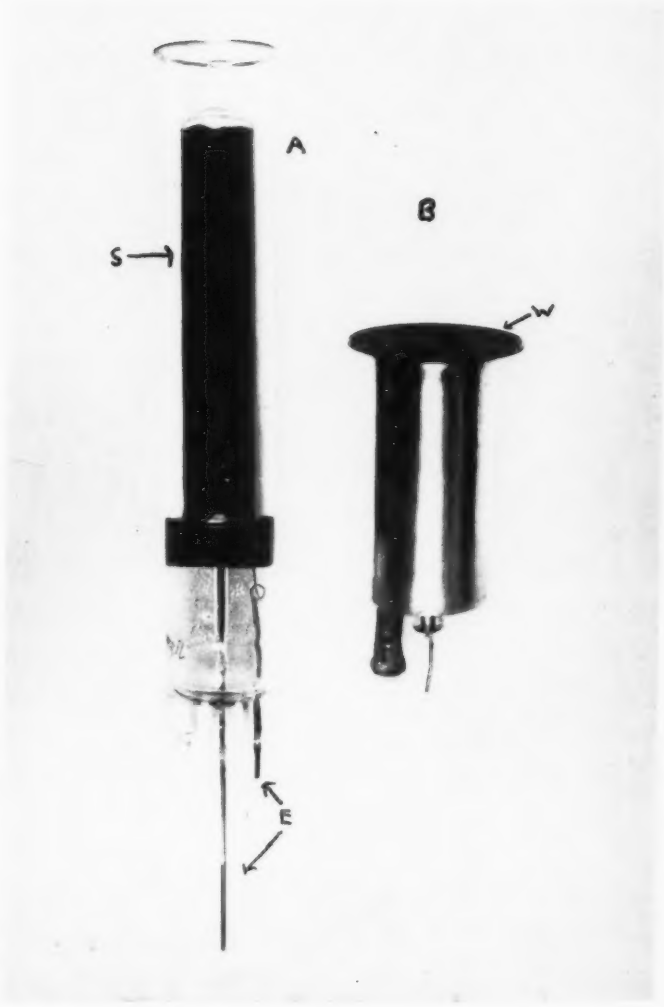


FIG. 1.

Two typical modifications of the Geiger-Muller tube:
(A) Is designed for the assay of radioactive liquids. The liquid is introduced into the annular space S. High potential is applied across the electrodes E. The black core is a thin-walled tube containing a gas/vapour mixture at low pressure through which pass ionising particles from the annular space.
(B) Is designed for the assay of solid samples. The sample is placed near the thin window W and particles from it ionise the gases contained in the metal cylinder.

F. H.

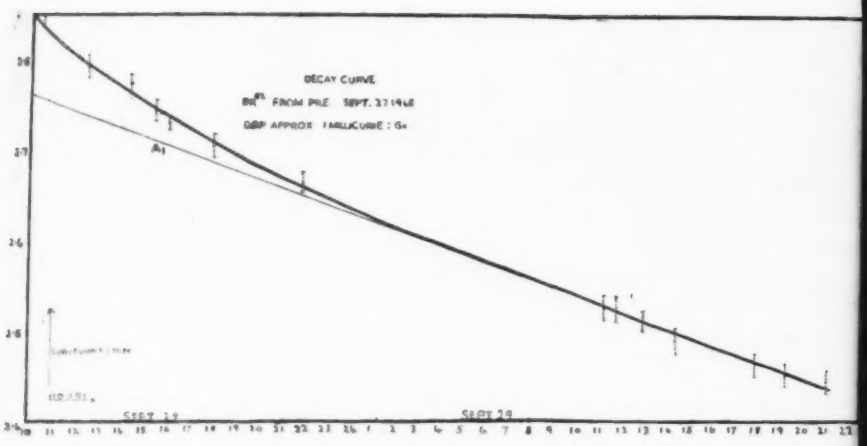


FIG. 2.

The loss of radioactivity of a sample of Br^{82} is indicated. The curve above the line A1 indicates that there is a contamination of the sample with a short-lived isotope of bromine.

FIG. 3.

A section of spinal cord has been placed upon photographic film. Around the cord there was a quantity of radioactive spinal anæsthetic. The anæsthetic affected the film. Two prints are shown.

F. H.

1. *Background.* A G.M. tube has a natural counting rate in the absence of any radioactive sample in its vicinity. This is termed ' background ' and its determined value must be subtracted from any estimated counting rate.

2. *Half-life.* The general technique of radioassay is to compare the counting rate of the test sample with that of a standard of known concentration. If the half-life is such that the drop in counting rate is insignificant during the time of the experiment, no correction need be made. If not, however, a decay curve must be constructed (Fig. 2), and with the aid of the curve the counting rate of the test sample can be compared with that of the standard at the time when the former was assayed.

3. Where the counting rate is high, the counter tends to " miss " a proportion of impulses. Allowance must be made for this.

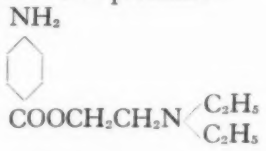
4. It is sometimes necessary to correct the apparent counting rate for B-particles absorbed by the medium in which the sample is contained, unless the medium is similar for successive samples.

5. It is essential to bear in mind the fact that nuclear disintegration is a random process and hence governed by statistical laws. Thus, even in the same sample, one cannot expect the ascertained counting rates to be identical in successive assays. The error should always be in terms of the S.D., which is defined as the square root of the number of counts. If the counting rate be low, however, then the error in background estimation must also be taken into account. It is not desirable to estimate a counting rate of less than 20% of background.

Application to a Problem

The author was interested in the fate of a spinal anæsthetic, the route by which it left the theca, the nature of its tissue

distribution and the channels by which it was excreted. The drug under consideration was procaine:—



Why an Isotope?

The first step was to devise a suitable method for the assay of procaine. A chemical method was the obvious choice. Those methods based upon the diazo reaction are probably the most widely used for procaine assay, Bullock and Macdonald (1938) claiming satisfactory results with concentrations of above 0.02%, while Kustner and Eissner (1930) and Willstaedt (1934) claimed a sensitivity to 0.01 mg. and 0.005 mg. respectively for their techniques.

It is evident, however, assuming a uniform tissue distribution, that the maximal tissue concentration in a 3000 g. cat after intrathecal injection of 1 ml. of 5% procaine HCl solution will be of the order 0.002%, and this figure assumes no excretion and no special absorption by any tissue. Even in the blood Bullock and Macdonald (1938) found that the procaine concentration was too low to be calculated accurately, although Goldberg et al. (1943) were able to make some estimations by the use of a different technique. This method of approach was thus unsatisfactory, for, even if the drug were present in adequate concentration for assay, it would still require laborious extraction procedures with some inevitable losses. Thus, since the administration of excessive doses was undesirable, an isotope method seemed indicated as it combines the virtues of greater sensitivity and, within limits, an indifference to the medium in which it is assayed.

Which Isotope?

In deciding which isotope would best serve the purpose a number of factors had to be borne in mind, among which may be mentioned:

(1) Availability,
(2) Half-life,
(3) Specific activity,
(4) Ease of synthesis of the final compound,
(5) Ease of assay.

These factors must be taken into account in any proposed tracer experiment, especially where it is intended to tag an organic molecule. In any particular example the factors will usually overlap. In the case of procaine, although it is possible theoretically to substitute any atom by its radioactive counterpart, when this research commenced all were unsuitable. Thus oxygen and nitrogen were inadmissable since their half-lives are each less than 10 minutes, leaving no time for the necessary synthesis. Of the unstable isotopes of carbon, C^{14} has a half-life of 4,700 years, but the beta particles are emitted at such low energy as to require special methods of assay, while its specific activity was of a relatively low order. The supply of C^{14} was also uncertain, while the synthesis itself promised to be troublesome. Similar objections applied to hydrogen.

A more fruitful line of approach in this particular case was the introduction of some other radioactive element into the procaine molecule without radically changing the pharmacological properties of the latter. The halogens appeared to be the obvious choice. Of the latter Cl^{36} can be prepared at low specific activity only, while the fluorines are too short lived to be of much value. The iodine group from a physical point of view is ideal, but the iodination of procaine is troublesome There remains bromine, and of the bromines, Br^{82} has a half-life of 34 hours and emits beta particles of maximum energy 0.465 M.E.V. each accompanied by three gamma rays of 0.547, 0.787 and 1.35 M.E.V. This suggests the assay of bromine to be relatively simple, though the half-period indicates that the work must be carried out speedily.

Where must the Isotope be Introduced?

The benzene ring is the easiest part of the molecule to 'tag' from the chemical point of view, and the nuclear halogens commend themselves since Williams (1947) and Fromherz (1928) have indicated them to be a stable group within the body. No matter what modification is suffered by the total molecule during its metabolism, bromine atoms will still be detectable and will represent the benzene nucleus to which they are attached. Morel et al. (1929) have prepared a dibromo-procaine (D.B.P.) using stable bromine and their method could be readily modified to suit the occasion (Howarth, 1948). A difficulty appeared later since it was found that the specific activity of potassium bromide obtained with the aid of the available cyclotron and the uranium pile was inadequate to produce a suitable degree of radioactivity in the dibromo-procaine. It thus became necessary to increase the radioactivity of the samples by the use of the Szilard-Chalmers (1934) extraction process after the irradiation of an organic bromine in the uranium pile.

Is the tracer firmly attached to the molecule?

If a tracer for any organic molecule is liable to be detached from this molecule, it is evident that its value as a tracer will be reduced. Although, as mentioned previously, the stability of the halogens seemed assured, it was necessary to confirm this, since the stability depends in part upon the configuration of the molecule and this was unknown during the final metabolic phases of dibromo-procaine.

Removal of ionisable products

It is necessary to be sure that after the particular synthetic procedure employed none of the tracer atoms are ionisable. In this case after bromination, some of the bromine appeared as D.B.P. hydrobromide, and the bromine in the hydrobromide was both radioactive and ionisable. This " free " bromine had to be removed prior to the biological work so that the only bromine in the molecule was incorporated in the benzene ring.

Pharmacology of the "tagged" molecule

Although it is evident that the investigation is now of dibromo-procaine and not procaine, Morel et al. (1929) have shown that the former is a local anæsthetic, and it is reasonable to suppose that although its pharmacology may differ in detail from that of procaine, it will in general be similar. These workers, however, did not investigate dibromo-procaine as a spinal anæsthetic, and, since the author was interested in it only as such, it was necessary to prove this point (Howarth, 1949b).

Method of assay: (a) With G.M. tube

The type of G.M. tube designed for the assay of liquid samples was selected for these studies. There were many reasons for this choice. For instance the position of the sample with relation to the window of the Geiger-Muller counter is critical, whereas in the case of the liquid counter the geometry is fixed. Again, more material can be presented to the sensitive volume of the liquid counter than in the case of the window-type Geiger-Muller counter, which is an advantage in the assay of low concentrations. In the liquid counter, however, it is necessary to present the sample in a suitable liquid medium. For this purpose lithium hydroxide was found to be satisfactory (Howarth, 1949a); it also proved suitable for similar brominated benzene compounds. The nature of a suspending medium varies with the chemical form of the substance to be assayed, and an appropriate one must be chosen in each case as it is necessary that the element under investigation be presented in a uniform manner to the sensitive volume of the tube.

Accuracy of radioassay

It is frequently desirable to check the accuracy of a particular assay technique by a suitable chemical method where this is available. In the present case radioassay was checked against the familiar diazo method for samples of the drug in C.S.F.

Method of assay: (b) Radioautography

A photographic emulsion responds in a similar manner to both light and the radiations from radioactive substances. It requires some 10^6 beta particles per sq. cm. to make an effective autograph but gamma rays are less efficient in this respect. Thus, to examine the distribution of a radioactive substance in a specimen of tissue, it is only necessary to cut a thin microscopical section of the tissue, and place the latter upon a photographic film for a period dependent upon the amount of isotope in the tissue, the film sensitivity, the half-life of the isotope and the nature of the radiation and then process the film in the usual manner. In this way a negative is obtained bearing a pattern similar to that of the isotope in the tissue. In practice, however, there are a number of difficulties. The resolution of such a trace is relatively poor, since the radioactive substance emits radiations in all directions so that each particle, instead of casting a precise shadow, produces a variable degree of halo. This halo can be reduced by closer approximation of tissue and film. It follows that the section itself must be extremely thin, but this also reduces the amount of isotope present. The grain size of the emulsion also influences the definition of the autograph, but if the grain size is small then the period of exposure must be increased. In practice a balance must be struck between these factors. Another factor often ignored is the nature of the histological processing prior to sectioning. It is essential that this should not remove any of the tracer substances from the tissue. Autographs were made in the study of D.B.P. and Figure 3 shows a radioactive anæsthetic around the section of the spinal cord. These autographs could be much improved by the techniques described subsequent to the completion of this work. For most problems the autograph techniques are subsidiary to the more precise methods of radioassay.

Biological effects of radiation

These effects must be considered in relationship to the biological processes of both the investigator and the problem in-

vestigated. A discussion of radiation hazards cannot be included here (see Lawrence and Hamilton 1948) and it must suffice that the first consideration in any tracer procedure is the health of exposed personnel. In the D.B.P. problem, Br^{82} emits both beta and gamma radiation. The beta particles give little trouble since these can be absorbed by the walls of a covered container, but the gamma, possessing considerable penetrating power, present more difficulty. Thus at one foot from one millicurie of Br^{82} the radiation dosage is about 128 milliroentgens per 8 hours exposure. A commonly given value for the tolerance dose is 100 milliroentgens per 8 hours exposure. The initial activity of the ethylene dibromide sample, from which the bromine for the bromination was obtained, was of the order of 500 millicuries and hence careful attention to health protection was essential, especially as a continuous 20 hour working period was not uncommon. The milliroentgen is one thousandth of a roentgen, which is that dose of gamma or X-rays which produces in 1 ml. of air under standard conditions a charge in ions of one sign equivalent to one electrostatic unit. In general, the cause of safety is best served when the operator's relationships with the isotopes are as brief, as distant, and as clean as possible.

The effect of radiation upon the biological system investigated presents a more difficult problem. It is certain that, as the activity of a tracer rises in a tissue, so will that tissue suffer increasing damage, until the results obtained in any particular experiment may be materially effected. Just when this is likely to occur depends among other things upon the radiation dosage received by the tissue and the sensitivity of the tissue itself. The information available in this particular field is sparse, and in practice it is desirable to check the isotope results against another method of assay, which course is often impracticable, since otherwise an isotope would probably not have been employed. Frequently it is necessary to employ some other device such as a comparison of the results obtained with doses of varying activity. This latter method was a technique employed

in the D.B.P. study. For a detailed account of the results obtained in the studies with a radioactive spinal anæsthetic see Howarth (1949 a and b).

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THE RELATIVE SUSCEPTIBILITY OF THE DIAPHRAGM, AS COMPARED WITH THE LIMB MUSCLES, TO THE EFFECTS OF TUBOCURARINE CHLORIDE

By J. D. P. Graham, M.D., B.Sc., M.R.C.P.E. and
R. St. A. Heathcote, M.A., D.M., B.Sc., F.R.C.P.

IN the classical accounts of the action of curare on the mammal, a definite order in which paralysis occurs in different muscles is agreed by all observers. The first to be affected are the short muscles of the toes with those of the eye and ear, then those in the limbs, next those in the trunk, and, finally, the diaphragm. In the earlier stages the paralysis of any muscle is not complete in that, at a time when no sustained tetanic contraction can be elicited, a response in the form of a " twitch " may still occur. It is the failure of the tetanic contraction which causes the poisoned animal to fall to the ground, although even then it may still be able to move its limbs.

Why there should be this sequence in the onset of paralysis, and why in particular the diaphragm should be the last muscle affected, is still unknown. Explanations have been offered for the relative insusceptibility of the diaphragm as compared with the limb muscles, but none seems entirely satisfactory. It has been suggested that the known difference between the diaphragm, a red muscle, and the limb muscles, chiefly white, is enough to account for the difference in susceptibility. On the other hand it may be argued that, while this difference undoubtedly exists, the action of tubocurarine is not upon the fibres themselves, but rather upon some undetermined point in a chain reaction occurring between the anatomical nerve ending, the end-plate, and the muscle fibre. So far as we are aware, little or nothing is known about any difference in that

chain reaction in red, as opposed to white, muscles. Again it has been argued that the diaphragm is a muscle of intermittent activity, and that the intervening short periods of rest are sufficient for the restoration of its function, while the limb muscles, or some of them, are required to be continually in action if the animal is to remain on its feet. This argument, however, applies equally forcibly to the limb muscles, as it has been shown conclusively by the Cambridge School that the absence of fatigue in these muscles is due to the fact that a proportion only of the fibres is in action at any time, and so the duty of maintaining posture is shared by all the fibres acting in groups, as it were in relays. There is, then, an intermittency in the activity of the limb muscles, as well as of the diaphragm.

It occurred to us that the difference in susceptibility of these muscles might be rather apparent than real. The needs of the body for gaseous exchanges through the lungs determine the extent of the respiratory movements, and so of the activity of the diaphragm. In an animal rendered immobile by curare or by an anæsthetic these needs will be reduced to a minimum, and it seemed not impossible that such minimal requirements might be met by a very greatly reduced power of movement of the diaphragm, in fact by a diaphragm which had been weakened to an extent comparable with that of the limb muscles when they became unable to sustain the weight of the body.

As we were unaware of any previous work in which a direct comparison of the effects of tubocurarine chloride on the power of the diaphragm and of the limb muscles had been made, this investigation was set on foot. When, however, this work was nearing completion, an account of an investigation with a somewhat similar line of approach appeared (Mushin, Wien, Mason and Langston, 1949). As the result of our observations, we have to admit that our original idea has been completely disproved, and that there is an inherent difference in susceptibility to the action of tubocurarine chloride between the diaphragm and the limb muscles.

Experimental Methods

In one section of the work, rabbits lightly anæsthetised with sodium pentobarbitone were employed. The greater part, however, has been done on cats, either decerebrate or under light chloralose anæsthesia. At the commencement attempts were made to use the decapitate animal but these failed, owing as it seemed to the low systemic blood pressure, inevitable with this preparation, giving an insufficient supply to the muscles.

In the first section the thorax of the decerebrate cat was opened under artificial respiration and both phrenic nerves were cleared and cut as high up as possible in the chest. Sherrington's preparation of the tibialis anticus muscle was adopted and its motor nerve also cut as high up as possible. The contractions of the two muscles were recorded by connecting the tendons to levers working against suitably adjusted springs, care being taken to avoid "afterloading" of the muscles. Two pairs of electrodes, connected in series to ensure equality in intensity of stimulation, were attached to the secondary terminals of an ordinary Dubois-Raymond coil. To avoid any risk of polarisation phenomena arising, the primary coil was supplied with alternating current suitably transformed down from the mains.

In the second section rabbits only were employed. A limb muscle, either the tibialis anticus or occasionally the gastrocnemius, and its motor nerve were prepared as before. The normally occurring movements of the diaphragm, in contrast to those artificially produced as in the former section, were recorded.

In the last section the spinal cord of cats, either decerebate or anæsthetised, was cut at about the 10th dorsal segment. On one side a motor nerve and muscle was prepared as before, either the tibialis anticus or gastrocnemius being employed. On the other side the posterior tibial nerve was cut low down in the thigh and the tibialis anticus tendon prepared for re-

cording, as the flexor reflexes are less affected by transection of the cord. Electrodes, in series as before, were applied to the sensory nerve on one side and to the motor nerve on the other so that the effects of stimulation of a muscle by a reflex and by a motor nerve could be compared.

In all cases the blood pressure was recorded from a common carotid artery, and an external jugular vein was cannulated for intravenous injection.

Experimental Results

Section 1

Faradic stimulation of five seconds duration was applied every half minute to the phrenic and anterior tibial nerves. When the height of the contraction of each of the two muscles appeared to be fairly constant, tubocurarine chloride was injected intravenously in small doses, repeated from time to time. Figure 1 shows a typical result. Immediately after the first injection of 0.1 mg., there was a diminution in the height of the contraction of the tibialis anticus with little or no change in that of the diaphragm. As the total amount of tubocurarine administered increased, there was a progressive diminution in the response of each muscle. Of the two, however, the tibialis anticus was much more affected than the diaphragm, as it proved almost unable to maintain any degree of tetanic contraction at a time when the diaphragm, although weakened, was still perfectly capable of giving an air exchange adequate for a motionless animal (see the fifth section of figure 1). With further injections of the drug even the " twitch " response of the tibialis anticus became practically abolished, but at this stage the tetanic response of the diaphragm had also gone.

On the injection of physostigmine in small amounts recovery commenced in both muscles almost at once but was much more complete in the diaphragm than in the tibialis anticus at the close of the experiment. The height of the contraction of the diaphragm had returned to almost one half of

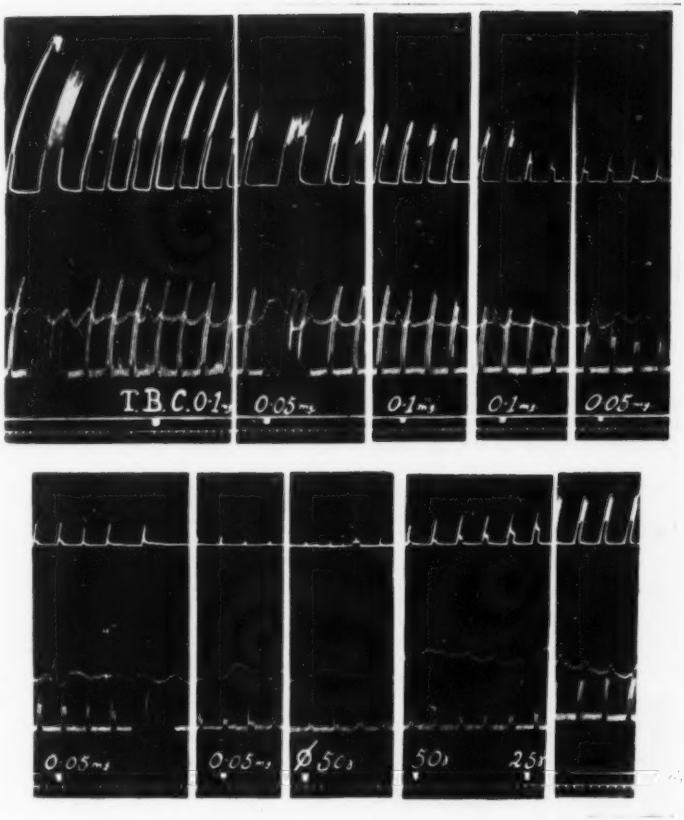

FIG. 1

Cat, 4 kgm., decerebate. Upper tracing, tibialis anticus; lower, diaphragm. Running through the latter is the blood pressure record. Next to bottom line indicates zero blood pressure. Bottom line, time tracing at 10 sec. intervals. In each of the first seven sections an injection of tubocurarine chloride in amounts as shown on the figure was made. Three injections of 0.05, 0.05, and 0.025 mg. of physostigmine and one of 1 mg. of atropine were given subsequently. For description see text.

G. & H.

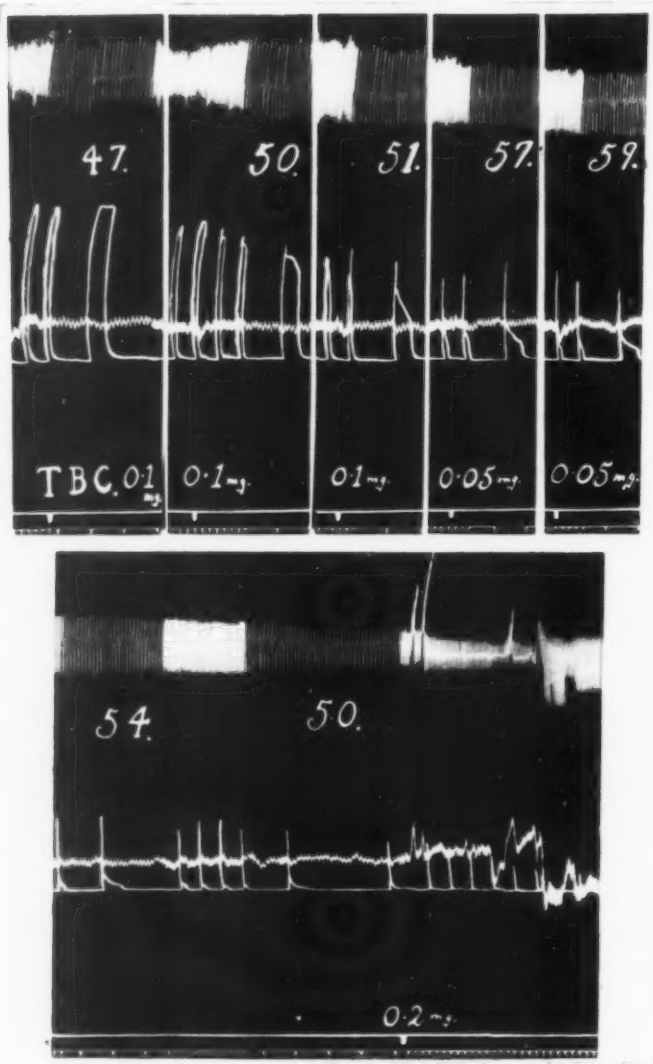

FIG. 2

Rabbit, 3.2 kgm., sodium pentobarbitone. Top record, diaphragmatic respiratory movements, the figures representing frequency per minute. Second record, blood pressure, steady almost throughout at 120 mm. Hg. Third record, contractions of gastrocnemius muscle. Lowest two lines, as FIG. 1. The figures at the injection points are total doses of tubocurarine chloride given. Before the first section an amount of 0.175 mg. had been given with atropine. A further 0.1 mg. was given between sections 5 and 6. For description see text.

G. & H.

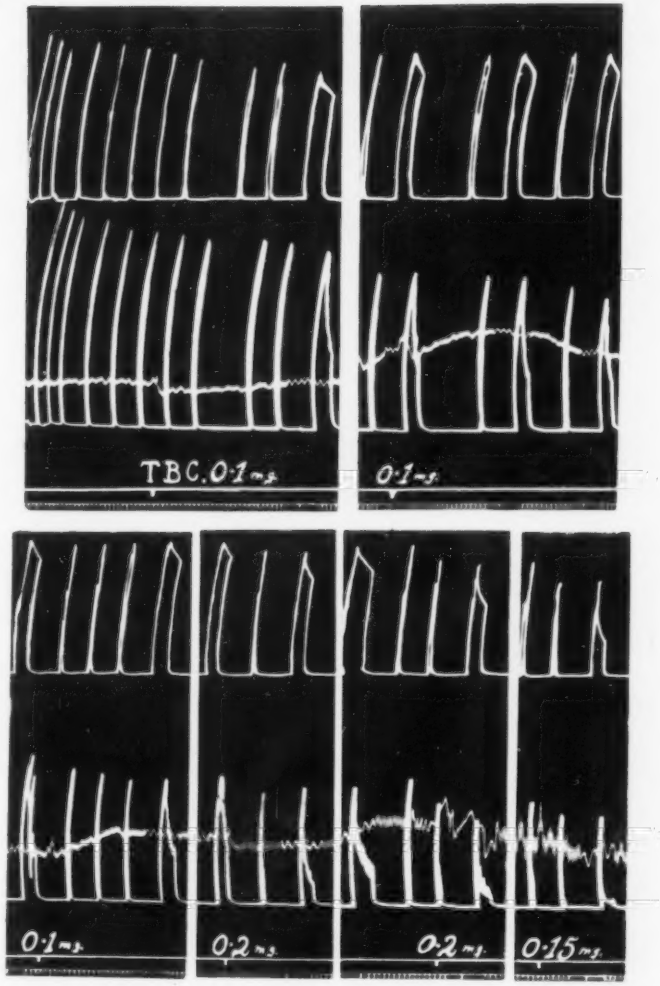

FIG. 3

Cat, 2.3 kgm., decerebate and spinal cord cut. Upper tracing, contraction of tibialis anticus on stimulation of motor nerve; second tracing, contraction of tibialis anticus on reflex stimulation. Cutting across the latter is the blood pressure record, 75–80 mm. at the start, rising to 110 mm., then varying from 75–100 mm. Hg. Lowest two lines, as in Fig. 1. Doses of tubocurarine chloride as marked are total doses given. For description see text.

G. & H.

that at the commencement, while that of the tibialis anticus had recovered to less than one third.

Throughout the experiment the blood pressure remained very constant at about 80 mm. Hg, until near the end when it rose to about 100 mm., due to the administration of atropine, used to counteract the circulatory side-actions of physostigmine.

Section 2

It was desired to obtain a state of considerable paresis in the limb muscles, but not actual paralysis, and to determine to what extent the normal respiratory excursions of the diaphragm would be diminished as a result. It was thought that the " head-drop " dose would be appropriate for this purpose. This dose was therefore determined in a few animals, and this amount was injected into an anæsthetised rabbit. It was found, however, that when given to an anæsthetised animal the " head-drop " dose was far too large, causing almost instant paralysis of the limb muscles, although the respiration was not arrested immediately. This was repeated with the same result in a second animal.

In later experiments, therefore, repeated small doses were given causing gradual onset of paralysis, as in the first section. Owing to the time taken up by the injections and by the observation of the effects of each, much of the drug was excreted. This fact, together with the known lesser effect of a given amount of curare when given in multiple doses rather than all in one dose, caused a total dosage to be used much greater than the estimated " head-drop " dose.

The general picture is shown in Figure 2. Small amounts, totalling 0.175 mg., had been given at a stage earlier than that shown in the beginning of the tracing. As a sharp fall of blood pressure had followed each injection of tubocurarine, atropine had also been given. It will be seen that, at the beginning, the tetanic response of the gastrocnemius was well maintained throughout the five second period of stimulation. At this time,

the respiratory rate was 47 per minute, and the excursion of the lever attached to the diaphragm measured about 19 mm. With further doses the height of the record from the gastrocnemius gradually became less, and the maintenance of tetanus steadily more impaired. When the total dosage had reached 0.525 mg., the height of the " twitch " part had been reduced to one half, but that of the tetanic part of the gastrocnemius record to only one tenth of the original. At the same time the respiration was still perfectly adequate, the rate being 57 per minute and the lever excursion measuring 18 mm. Another dose of 0.1 mg. reduced still further the tetanic response, although having little effect on the height of the " twitch ". In an attempt to abolish the latter a further 0.2 mg. was administered with the result that the last traces of tetanus were annulled, and the twitch reduced to about one eighth of the original height. At the same time, however, the diaphragm was greatly affected, the respiratory excursions becoming slower and weaker until they finally stopped.

Section 3

The object of this section was to determine whether tubocurarine chloride affects in a different manner the response of a muscle when stimulated through its motor nerve on the one hand and on the other reflexly by stimulation of a sensory nerve. A typical tracing is shown in Figure 3, although the blood pressure was less constant than might have been desired. It will be seen that the contraction in response to a sensory nerve stimulus was more quickly and more markedly affected than that caused by stimulation of the motor nerve. The " twitch " part of the contraction was reduced by the action of the drug in the two muscles in almost equal measure. The tetanic part of the reflexly induced contraction failed more quickly, however, so much so that it was practically abolished at a time when that caused by motor nerve stimulation was still one third as great as in the normal. This effect was observed in both the decerebrate and the anæsthetised cat,

although in the latter the difference between the two muscular responses was less marked.

Discussion

The results obtained in the first two sections of this work speak for themselves and little discussion is needed. They show clearly that when the diaphragm and a limb muscle, under exactly similar conditions, are exposed to the action of tubocurarine chloride, the former muscle is more resistant to the drug. This is true whether both muscles receive their stimulus in the form of faradic currents applied to the motor nerve, or the limb muscle alone receives such stimulation while the diaphragm is responding to the normal form of stimulation. The difference in susceptibility was not found to be very great, of the order of 4 : 5. An analogy may perhaps be sought in the reactions of unstriated muscle to drugs. There is little apparent histological difference in the smooth muscle fibres of the various organs of the body. None the less, great differences exist in their reactions to drugs. Thus the blood vessels are readily affected by the nitrites at a concentration which is without action on the bronchial musculature. Again, the blood vessels are more sensitive than any other organ to the action of adrenaline.

The chief justification for the use of tubocurarine in anæsthesia is that it allows complete abolition of tone in the voluntary muscles at a relatively light level of anæsthesia. Tone in voluntary muscle being a reflex phenomenon, the third section of this work was undertaken to determine what effect tubocurarine might exert on the responses of muscles stimulated (*a*) through the motor nerve, and (*b*) by a reflex, and whether any difference might exist between the responses. It has been found that both responses are reduced by tubocurarine, but that the reflex is the more rapidly affected of the two. Now, it has been shown in the second section of this work that the diaphragm responding to its natural stimulus is less

affected by the drug than is the limb muscle, stimulated through its motor nerve. A fortiori, therefore, it should be relatively more capable of carrying on its necessary movements at a time when the reflex phenomenon of tone has been abolished.

An important aspect of the use of any potent drug is its therapeutic index, which in the case of tubocurarine would be the ratio of the dose required to arrest respiration to that needed to abolish muscular tone. From the first and second sections of this work we should estimate that the dose required to arrest respiration is about one fourth higher than that required to abolish the tetanic response to nerve stimulation in a voluntary muscle. From our experiments on anæsthetised animals in the third section of this work, we conclude that there is little difference, about 10–20 per cent, in the dose required to abolish tetanic responses in muscles stimulated through the motor nerve and by a reflex. This would bring the therapeutic index of tubocurarine, as defined above, to about 1.4, a figure in sufficiently close agreement with that obtained by Mushin et al. (1949).

Summary

(1) Direct recording of the effects of tubocurarine chloride on the contractions of the diaphragm and and of a voluntary muscle has shown that the former, whether stimulated naturally or artificially through the phrenic nerve, is less susceptible to the drug than is the latter.

(2) Similarly, it has been shown that the response of voluntary muscle to a reflex stimulation is more readily affected by tubocurarine chloride than is its response to stimulation of its motor nerve.

(3) The therapeutic index of the drug is estimated as being about 1.4.

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A PRACTICAL MEANS OF DETERMINING CO_2 CONCENTRATIONS IN SAMPLES OF ANÆSTHETIC AND OTHER GASES

By

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Introduction

FOR some years we have been interested in the effects of CO_2 during anæsthesia but we have been unable to investigate them, because there was no practical means of estimating this gas in the presence of other anæsthetic gases. The general use of drugs which can cause profound effects on respiratory movements, and the widespread use of CO_2 absorption has created a real need for some simple and reasonably accurate means for estimating CO_2 *in the operating theatre*. The methods at present available in the laboratory are not practicable.

We are fortunate in that one of us (H.T.R.) has for a number of years been actively engaged in the manufacture of instruments for recording the concentration of various gases, and the principle of the indicator which we are about to describe is a modification of the Ringrose system of automatic mine gas measurement, approved by all the chief coal producing countries. With modifications it is capable of application to almost all gases and vapours with an accuracy approaching chemical analysis.

We have demonstrated the use of a CO_2 indicator before the Physiological Society meeting held at Leeds on September 24th, 1949. We learnt that this device could be applied with advantage to other branches of Medicine, for instance, as a rapid

method to show the activity of soda lime used in metabolic apparatus.

The R.R.H. CO_2 Indicator for Use During Anæsthesia

The R.R.H. CO_2 indicator (Fig. 1) is designed to show the percentage of CO_2 in the presence of any varying mixture of anæsthetic gases. It can be used either continuously or intermittently and the changes in CO_2 concentration are shown quickly. The readings are large, about ¾″ of manometer reading for each 1% of CO_2, and can therefore be seen at a considerable distance.

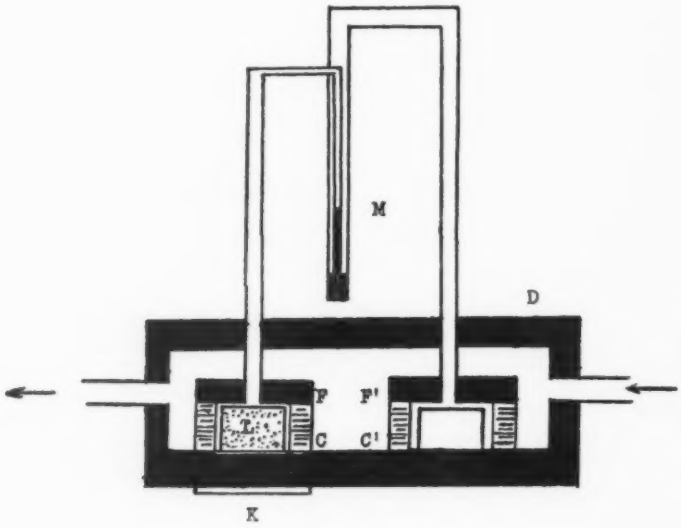
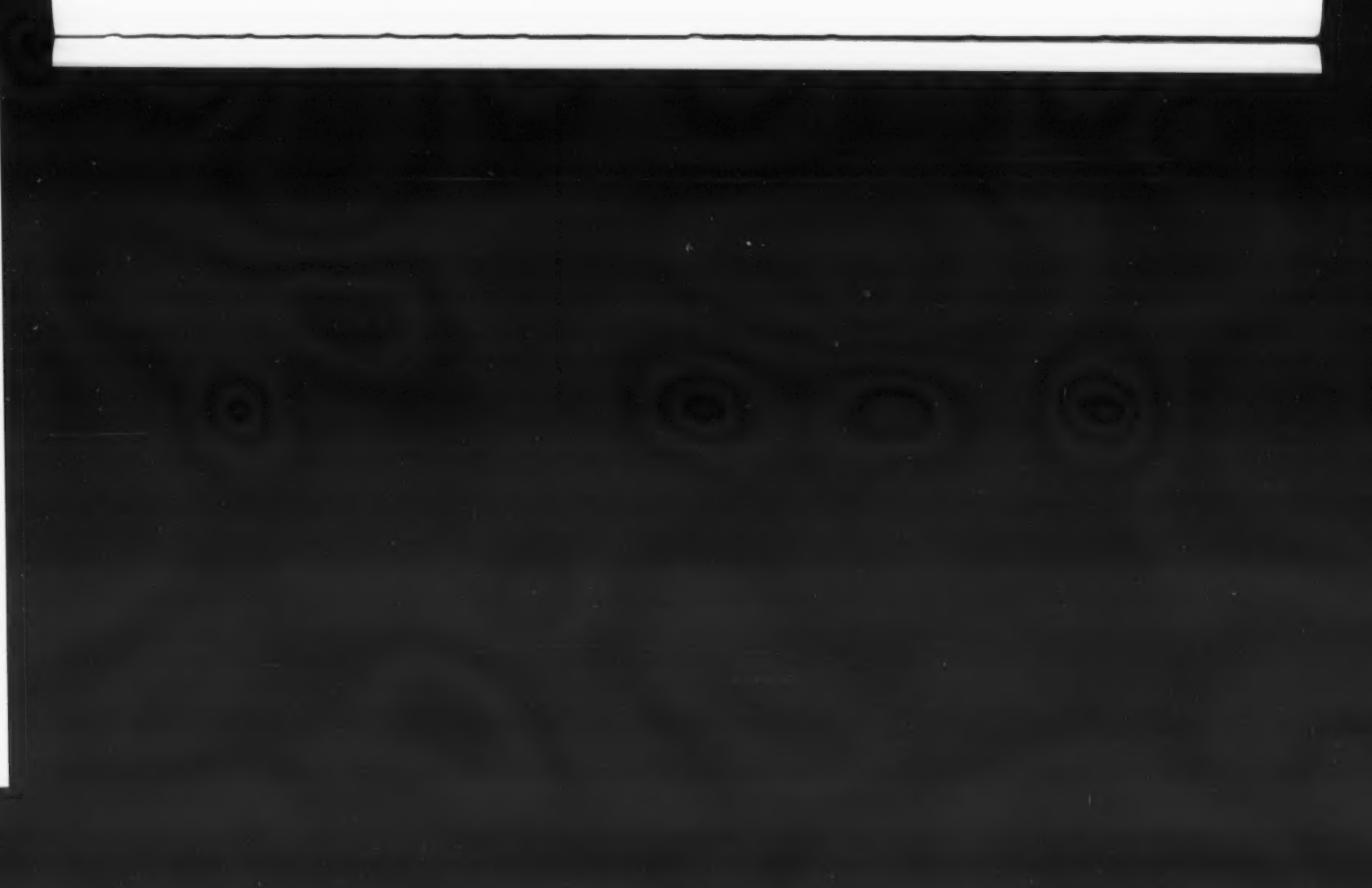


FIG. 2

Principle of the R.R.H. CO_2 Indicator

Two porous unglazed porcelain cylinders C & C′ (Fig. 2) are suitably mounted by metal caps F & F′ in such a way that they are air-tight except for the porosity of their walls. One



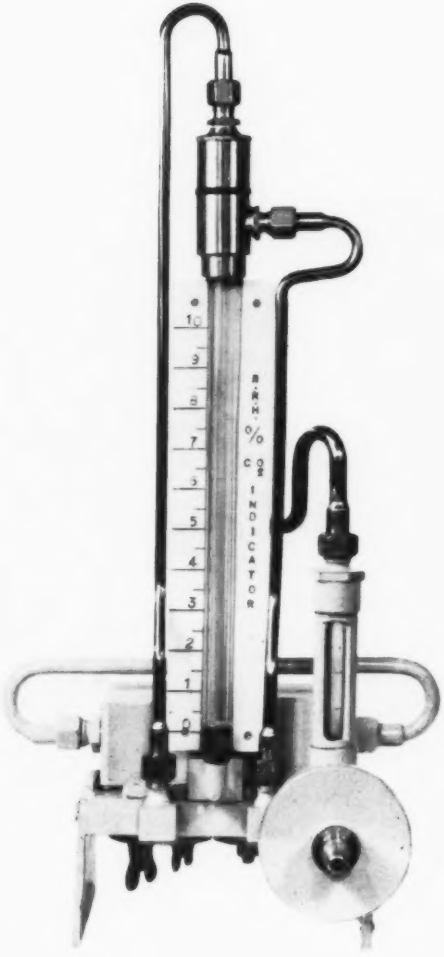


FIG. 1

H. T. R.

of the cylinders is provided with a removable cap K on which is mounted a gauze cylinder into which can be placed a quantity of non-hygroscopic soda lime L; the other cylinder is filled with material which does not absorb CO_2 but which occupies approximately the same volume as the soda lime. Tubes attached to the interior of the porous vessels are joined to a differential pressure measuring device M, such as a U tube manometer, and hence any difference in pressure in the porous vessels is easily shown by difference in level of the liquid in the legs of the U tube. The whole of these vessels is enclosed by a covering made air-tight and into which the atmosphere under observation can either be blown or aspirated.

Assuming the atmosphere under test is air mixed with some CO_2, then absorption of CO_2 which diffuses from the outside to the inside of porous cylinder C occurs, and a drop in pressure is shown depending on the concentration of CO_2. No absorption occurs in C′ and in this particular case the porous cylinder C′ is unnecessary.

If, however, the atmosphere under observation contains, in addition to CO_2, varying amounts of chloroform, ether, cyclopropane, trichlorethylene, or nitrous oxide and oxygen then the porous cylinder C′ is essential to negative their presence.

Owing to the varying densities of the anæsthetic gases the rates of diffusion must be made the same in both porous cylinders, and, if the cylinder C has its CO_2 absorbent removed, there should be practically no differential pressure set up when the atmosphere containing the anæsthetics is passed through the apparatus. Any slight change in pressure soon rights itself. Should, however, the porous cylinder C contain its absorbent (soda lime), then the balance of pressure is upset, and a reading of CO_2 percentage is given quite irrespective of the presence of varying concentrations of anæsthetic vapours or gases.

As applied in practice, it is customary to use slight positive pressure to pass a sample through the flowmeter (Fig. 1), which should indicate at least half way up, and thence into the container D surrounding the porous cylinder. To remove

excessive moisture from the sample it is necessary to place in the container attached to the flowmeter some calcium chloride, otherwise the flowmeter may temporarily stick. The soda lime should be changed every day the apparatus is used; this will ensure its efficiency under all circumstances. Means are provided on the device for filling the liquid in the manometer and setting the zero of the scale, and the liquid is practically unspillable.

Laboratory Tests

One of us (R.P.H.) has carried out a number of experiments to test the performance of this instrument under known conditions. This work was mainly done in the Physiology Department of the University of Leeds.

(1) The passage of nitrous oxide, oxygen, ether, chloroform, trichlorethylene or cyclopropane failed to raise the liquid in the recording manometer. An immediate rise occurred with CO_2.

(2) Mixtures of CO_2 in air were made up in a Douglas bag and circulated between it and the CO_2 indicator with an electrically driven air pump. A by-pass arrangement allowed the volume passing through the indicator to be controlled by means of a screw clamp. Samples of the bag mixture were tested in the Haldane gas analysis apparatus a few minutes before and after periods when readings were made with the CO_2 indicator. (See Fig. 3.)

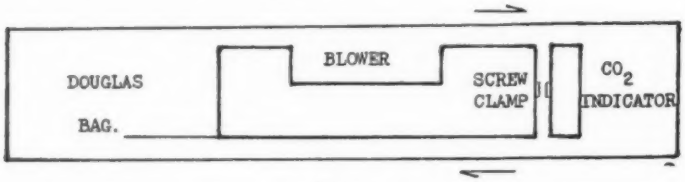


FIG. 3

Diagram showing the arrangements for laboratory tests

The correspondence between the readings of the CO_2 Indicator and the Haldane apparatus estimations of CO_2 is shown in Table I which represents a series of 12 experiments using the same sample of soda lime. This sample was used

TABLE I

Percentages of CO_2 in air determined by the Haldane apparatus compared with the highest and lowest values recorded by the R.R.H. CO_2 Indicator over varying periods of time, with mixtures circulating through it and a Douglas bag.

No. of expt.	Haldane 1	Haldane 2	R.R.H. 1	R.R.H. 2	Differences between Haldane & R.R.H.	Interval between R.R.H. 1 & 2 in minutes	Period of exposure of soda lime at end of experiment
1	3.1	2.76 2.76	3.2	2.7	0.1–0.1	130	2 hrs. 0 mins.
2	4.35 4.35	3.71 3.71	4.6	3.8	0.2–0.1	140	4 hrs. 30 mins.
3	3.99 3.98	3.36 3.36	4.05	3.4	0.1–0.0	130	6 hrs. 40 mins.
4	4.28 4.25	3.83 3.83	4.4	3.9	0.1–0.1	105	
5	4.8 4.7	4.57 4.57	4.65	4.5	0.1–0.1	39	9 hrs. 0 mins.
6	4.33 4.33	4.27 4.27	4.3	4.1	0.0–0.2	40	
7	5.45 5.45	5.25 5.25	5.25	5.0	0.2–0.3	65	11 hrs. 3 mins.
8	4.25 4.25	4.35 4.35	4.30	4.15	0.0–0.2	21	
9	1.52 1.52	1.41 1.41	1.5	1.38	0.0–0.0	56	
10	7.51 7.51	7.2 7.25	7.5	7.05	0.0–0.1	65	13 hrs. 30 mins.
11	7.6 7.6	7.36 7.36	7.4	7.2	0.2–0.2	50	
12	7.36	7.24	7.0	6.75	0.4–0.4	85	15 hrs. 0 mins.

each day for periods of approximately 2 hours. It was then rested for periods of approximately 24 hours (at one week-end the rest extended for 72 hours). The table shows that the readings of the indicator closely follow the results of the Haldane estimations.

Figure 4 represents one of these experiments graphically. It shows the rapid response, the Haldane level being reached in 3 minutes. Usually the time taken from zero to the peak was from 3 to 5 minutes. The gradual fall of the readings follows

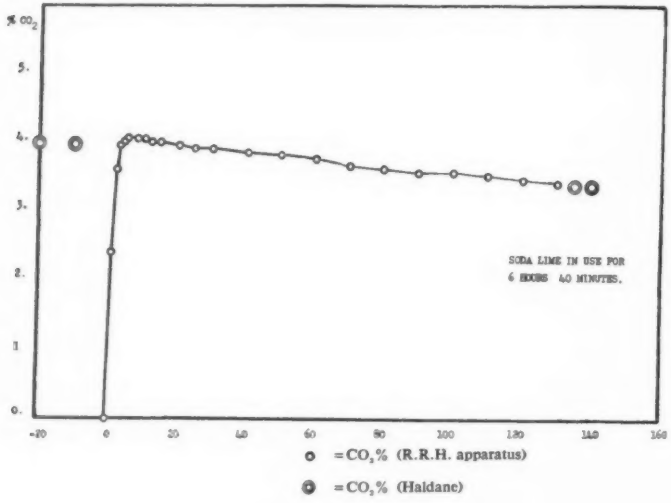


FIG. 4

Graphic illustration of the rapid response of the R.R.H. Indicator. Note that the Haldane level is reached within three minutes

a similar fall in the CO_2 concentration in the bag as confirmed by the Haldane tests. This represents a slight leakage of CO_2 through the bag walls.

Figure 5 shows how the CO_2 indicator responds rapidly to change. It was possible to change a Douglas bag within from 1–2 minutes.

Purpose

The purpose of this device is to give anæsthetists immediate, positive, and visible evidence of CO_2 accumulation from either (1) insufficient elimination of CO_2 due to reduced pulmonary

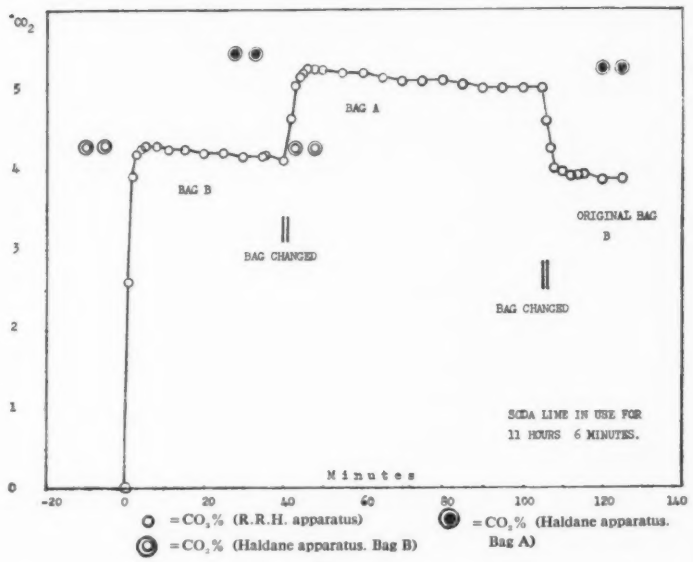


FIG. 5

Diagram to show rapid response of R.R.H. Indicator to change in concentration of CO_2

ventilation or (2) from inefficient absorption of CO_2 by exhausted soda lime in closed circuit apparatus, also (3) it can be used as an additional check when CO_2 gas is administered from a cylinder.

Accessories to Anæsthetic Equipment for Use with the Indicator

The different types of anæsthetic equipment and the various purposes for which the indicator can be used create the need for the construction of several pieces of apparatus for sampling respired gases.

The indicator may be connected with anæsthetic apparatus by means of rubber tubing to outlet ports specially constructed with " on " and " off " taps. They have been incorporated with

(1) endotracheal mounts, (2) face-piece angle mounts, (3) the inspiratory limb tubing mount for circle CO_2 absorption equipment, and (4) the bag mount connecting the reservoir bag and Waters' absorber.

When used as above the sample passes through the indicator and into the atmosphere. This is a disadvantage in the case of expensive and explosive gases. Further apparatus is at the present time under construction, which enables the sample to be returned into the respired system with provision for intermittent or continuous use.

Application to Anæsthesia Administration

The R.R.H. indicator has been in use for the past six months under practical conditions. It is too early to draw conclusions from such data as has been obtained. One of us (R.P.H.) has been conducting anæsthesia for major thoracic surgery with intravenous thiopentone, Tubarine and endotracheal nitrous oxide, oxygen inhalation by the " to and fro " Waters' method of CO_2 absorption. When the indicator reveals a progressive rise in CO_2 (endotracheal mount sample) it has been found that the patient's respiratory movements decrease *if respiration be aided by manual bag compressions using an increased flow rate and a partially open expiratory valve.* Controlled respiration can now be performed at a lighter plane of anæsthesia and the bleeding from cut surfaces appears to be reduced. One of our surgeons asked if the patient's condition was satisfactory, because of the absence of the usual amount of bleeding. We have found that there have been instances when we would normally have given additional doses of barbiturate intravenously to decrease respiratory volume. With this new technique, however, and by watching the indicator, we have been able to distinguish more readily between the deep breathing which is due to the inhalation of excess of CO_2 and that which is due to light anæsthesia, and we have been able to avoid unnecessary additions of barbiturate, with the result that, particularly towards the end of operation, we have been able

to conduct the administration so that the reflexes returned soon after operation. It is a great advantage during anæsthesia to be able to ensure that respiratory movements resemble those of normal breathing in the conscious state and for bleeding to be cut down to a minimum.

Conclusions

There is at present no other practical device which can be used continuously during anæsthesia to measure the concentration of carbon dioxide in the presence of anæsthetic mixtures.

We believe that the routine use of this instrument by anæsthetists will greatly increase the precision of inhalational anæsthesia.

Acknowledgements

We wish to thank Professor Hemingway for the interest which he has taken in our work, for placing laboratory facilities at our disposal, and for much valuable advice. We also thank Mr. Richard Teale who made the first instruments. The apparatus can be obtained from Messrs. A. Charles King Ltd., 27 Devonshire Street, London.

LOCAL ANÆSTHETIC SOLUTIONS

By R. Bryce-Smith, M.A., B.M., B.Ch., D.A.

WHEN a local anæsthetic is injected into the tissues and fails to achieve its purpose, the pH of the solution is often blamed as the underlying cause. This, and the contradictory statements (a) that in no circumstances must an alkali come into contact with local anæsthetic drugs, and (b) that by alkalinizing a local anæsthetic solution its activity may be increased, make the subject worthy of consideration.

Anæsthetic Failure

When sufficient alkali is added to a local anæsthetic solution, a dense white precipitate forms. This precipitate is composed of anæsthetic base which is insoluble in water. Its solubility in lipoids can be demonstrated by adding olive oil, shaking well and allowing to stand, after which two perfectly clear layers may be seen. Further addition of alkali to the aqueous portion will not cause precipitation, showing that all the local anæsthetic has been converted into base and dissolved in the oil; the aqueous moiety is in fact completely inactive.

The pH at which precipitation occurs varies with individual local anæsthetic drugs, and, equally important, with the concentrations of the solutions. Thus the addition of an alkali precipitates base more readily from a strong than from a weak concentration:

	pH at which precipitation occurs	
Strength of Solution	1 : 100	1 : 1000
Amethocaine	pH 6.1	pH 9.1
Procaine	pH 8.4	—
Nupercaine	—	pH 6.5

This table explains why even a trace of alkali inactivates Nupercaine.

It follows that care must be exercised in the preparation of containers in which local anæsthetics are to be dissolved and in the sterilization of syringes. If these articles are boiled in tap water there may be considerable quantities of alkali present; and, if the water is hard, a fine film of carbonates will adhere to any surface. The addition of a trace of acid to the sterilizer will prevent this, and as an added precaution everything with which the local anæsthetic solution will come into contact should be rinsed in sterile distilled water or saline before use.

Commercial preparations of local anæsthetic drugs have their pH carefully standardized and are marketed in alkali free glass. This includes solutions for spinal anæsthesia but failure here may result from something beyond the anæsthetist's control. Cohen and Knight (1947) found considerable variation in the pH of the cerebro-spinal fluid of different individuals, and in exceptional cases it was high enough to precipitate the base from the spinal anæsthetic solution. Possibly an abnormality such as this accounted for the family reported by Sebrechts (1932) to be immune to local anæsthetic drugs injected intrathecally. At the other end of the pH scale of body fluids Light and Cooke (1928) found the figures for pus to be in the region of 5 to 6. The failure which often follows injections of local anæsthetics into infected areas, especially where pus is present, is discussed later in this article.

Sterilization and Storage

The sterilization of local anæsthetic drugs offers many problems, and it is obvious that these must be overcome by the chemist rather than the anæsthetist. The methods available are:

(1) heating by boiling, or autoclaving;
(2) heating to 80°C. for 30 minutes on four consecutive days;
(3) the addition of a chemical;
(4) bacterial filtration.

It might be expected that the melting points of the salts of local anæsthetic drugs would give an idea as to whether they will withstand heat sterilization, but this is not the case. For example, whilst aqueous solutions of cinchocaine hydrochloride (M.P. of crystals 90°C. to 98°C.) may be repeatedly boiled or autoclaved in sealed ampoules, there is some doubt whether procaine hydrochloride solution (M.P. of crystals 153°C. to 156°C.) may be boiled without causing some decomposition.

Solutions of most of the local anæsthetic drugs and in particular amethocaine (Bullock and Cannell, 1941) lose some of their potency when stored for prolonged periods, and this decomposition is aided by heat. The reaction, which is one of hydrolysis, occurs most readily in the higher pH ranges but is self-limiting, since the resulting shift to the acid side inhibits further decomposition. To prevent hydrolysis and loss of potency during storage, some commercially prepared solutions are intentionally acidulated. In some cases the added agent has been known to break down, lowering the pH still further. Such solutions may be highly irritant and cause pain and œdema at the site of injection (Wilson, MacDonald and Bullock, 1938). An offender in this respect is the B.P. preparation, Injectio Procainæ et Adrenalinæ, which contains 2% procaine and to which is added sodium metabisulphite. The latter gives the solution a pH of approximately 3.5, but during storage may break down into sulphuric and other acids (Tainter, 1941) rendering the preparation dangerously acid.

Adrenaline decomposes readily in an alkaline medium. If a local anæsthetic solution is made up with adrenaline and is to be stored it is all the more necessary to ensure that the pH is reasonably low. If a solution is required which is to be neutral or alkaline in reaction then it must be freshly prepared by the anæsthetist before use.

Alkalinized Solutions

The pH of a local anæsthetic solution may be raised by the addition of an alkali such as sodium bicarbonate. This will

allow hydrolysis in the tissues to occur more readily with the rapid liberation of local anæsthetic base, the form in which the drug is able to penetrate the nerve cell.

Bignon took advantage of this when, in 1892, he employed a solution which he called " cocaine milk " the turbidity of which was due to partial precipitation of the cocaine. He found that such solutions were more active than those usually employed, but later workers (Toelkens, 1914, Farr, 1923) found that they were often completely inactive, presumably due to total precipitation of the cocaine as a result of adding too much alkali.

The advantages which have been claimed at different times for local anæsthetic solutions which have been alkalinized immediately before use are:

(1) the onset of anæsthesia is more rapid;
(2) the duration is greater;
(3) a lower concentration of drug may be used to obtain the same results;
(4) they cause less pain and tissue irritation at the site of injection;
(5) they cause fewer systemic reactions.

The first three of these advantages have received substantial support from the animal work performed by Trevan and Boock (1927). In clinical practice the alkalinization of local anæsthetic solutions has been limited almost exclusively to dental nerve blocks. Even in this limited field there is considerable divergence of opinion for while Ahrens (1938) believes in all these advantages except in the increased duration of anæsthesia, Tainter, Throndson and Moose (1939) refute all the claims made for alkalinized solutions.

In general surgery a greater volume and more dilute solutions are used. The body fluids have remarkable buffering properties: it follows, therefore, that solutions injected into the body are rapidly brought into equilibrium with that of the tissue fluids. This buffering effect will be less noticeable as

the volume of the injected solution increases, and to minimize this effect still further the solution may itself be buffered. Unfortunately such solutions present difficulties in preparation and sterilization which prevent their everyday use.

It is not easy to form an opinion as to whether alkalinized solutions have a place in general surgery but at least it is reasonable to avoid highly acid solutions, and this implies that the solution should be freshly prepared.

Preparation of Anæsthetic Solution

The method of choice is to add a given weight of local anæsthetic, in the form of dry crystalline powder from a sterilized container, to sterile saline, such as that used in any transfusion service. 1/1000 adrenalin readily available in 0.5 ml. ampoules should be added at the same time. This method of preparing each solution freshly and independently has stood the test of time and has much to recommend it. The method is simple and the chances of infection are reduced to a minimum since all the components are sterilized by the manufacturers. The low pH of stock solutions is avoided and the pH of the freshly prepared solutions depends almost entirely on that of the saline employed.

In practice it is almost impossible for the anæsthetist to estimate the pH of his solution so that there is no means of adjusting it to any required level unless a purely empirical method, with its consequent dangers, is employed. Simple colour indicators cannot be used since many contain sulphones and phthaleins which are incompatible with local anæsthetics. An electric pH meter is expensive and, unless the operator has been specially trained, the apparatus is difficult to use. The only remaining procedure is the titration method of Michaelis, a description of which may be found in most textbooks of biochemistry.

Using this last method, I found that the pH variations of local anæsthetic solutions, prepared in the manner described above, were small. In 500 such solutions the range was between

pH 6 and pH 7.2. One point of interest was noted during these investigations. If the solution is prepared in an enamel jug, the pH rises steadily as long as the solution remains in the jug, but this phenomenon is not seen when the container is of chemically pure glass. Since a similar rise in pH occurs even when saline alone is placed in an enamel jug it is assumed that alkali is dissolved out of the enamel. Consequently there is a chance of precipitation occurring if a local anæsthetic solution is allowed to stand in the jug, and if such a container is to be used, then the solution must be prepared immediately before use. The rise in pH levels is more marked with rises in temperature, but even in normal working condition (20°C.) it is approximately one pH unit in forty-five minutes.

The Mode of Action of Local Anæsthetic

The full story is not yet known but some isolated facts point the way.

Fulton (1921) first attempted to unravel the problem by combining hæmotoxylin with Novocaine, and thereby produced a vital stain which he called Novocaine-brown. This dye penetrated the nuclei of nerve cells, but when applied to nerve fibres, staining did not occur although an effective nerve block resulted.

Various workers (Gros 1912, Sollman 1917, Beutner 1940, Lundy and Osterberg, 1928) agree that when local anæsthetics are injected into the body they undergo hydrolysis. The alkaline tissue fluids liberate the lipoid soluble local anæsthetic base, and the reaction may be typified by the following equation:

$$\text{Procaine HCl} + \text{NaHCO}_3 \rightarrow \text{Procaine base} + \text{NaCl} + \text{H}_2\text{CO}_3$$

Since all local anæsthetics are salts of basic substances this reaction is common to all. Consequently the weaker the base, the more ready the hydrolysis. Since these are aqueous solutions, ionization must occur concurrently. This reaction may be shown thus:

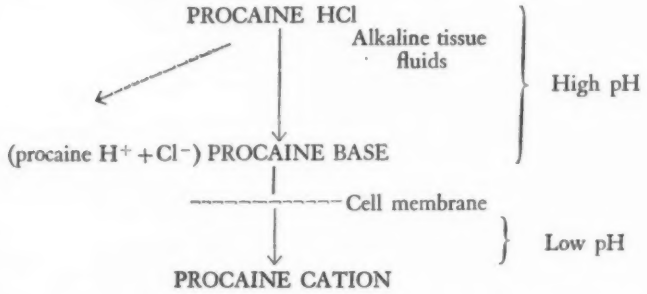
$$\text{Procaine HCl} \rightleftharpoons \text{Procaine}^+ + \text{Cl}^-$$

Ionization proceeds until a state of equilibrium as demonstrated above exists.

In 1940, Krahl, Keltch and Clowes pursued this problem using the motility and cessation of divisions of the larvæ and eggs of the sea urchin as standards of anæsthetic action. This work too confirmed that hydrolysis was the first step in a chain of events and it was shown that a local anæsthetic was able to penetrate the cell only in the form of the undissociated molecule. This reaction was hastened by raising the pH of the extra cellular medium—in other words by making it more alkaline.

Ionization was found to occur at the same time, although only to a small extent. The degree of ionization did, however, rise with the higher pH levels.

After entering the cell, the next step appeared to be a dissociation of the base, thereby producing a local anæsthetic cation. The rate of this reaction is dependent on the intra-cellular pH to which it is directly proportional. This cation was believed to be the essential factor in producing anæsthesia. Diagrammatically the sequence of events may be shown as follows:



A state of equilibrium arises between the undissociated molecules in the extra-cellular medium and the intra-cellular contents, and again between the undissociated molecules and the local anæsthetic cations within the cell.

It must be realized that the conditions of these experiments were necessarily artificial, and that, therefore, the results cannot

be accepted without further proof as representing the course of events within the human body.

The much quoted theory of Donaggio (1937) that local anæsthetics act by causing a primary reversible degeneration starting in the myelin sheath, does not appear to have any supportive evidence. That changes occur in the cell membrane is not doubted, e.g. local anæsthetics cause a lowering of the surface tension (Gardner and Semb, 1935), but this change does not run parallel with anæsthetic efficiency, although it is likely that the membrane permeability is altered. It is difficult to understand how a degeneration, in the generally accepted meaning of the term, can occur, because of the following facts:

(1) the rapid onset of anæsthesia, which would not allow sufficient time for such a reaction to take place;

(2) the unaltered consumption of oxygen by a blocked nerve at rest (Dawes, 1949). A considerable reduction would be expected if a degenerative process had occurred;

(3) if a blocked nerve is "washed" in saline thereby reducing the concentration of the local anæsthetic present, there is a rapid return of activity, and the nerve will again allow the passage of an impulse.

To summarize, the only confirmed facts known about the mode of action of local anæsthetics are:

(1) local anæsthetics penetrate the nerve cell only in the form of local anæsthetic base;

(2) hydrolysis of the local anæsthetic salt occurs most rapidly at the higher pH levels, and, conversely, may be inhibited at the lower levels;

(3) when a nerve is blocked, there is no reduction in the oxygen consumption of that nerve whilst it is at rest;

(4) when a nerve is blocked, there is a reduction in the action potential (Davis, Forbes, Brunswick and Hopkins, 1925);

(5) local anæsthetics cause a lowering of the surface tension;

(6) the application of the Overton theory of narcosis (Overton, 1901) to local anæsthetic drugs is valid and their efficiency follows their coefficient of solubility in oil (Gros, 1910).

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*BROWN OF ADELAIDE

By GEOFFREY KAY, M.D., F.F.A.R.S.C., D.A.

IF the reader of this paper were an Australian anæsthetist, he would find himself writing now and then to Adelaide, to seek the advice of an Elder Counsellor whose name is Gilbert Brown. From this very fact one may infer Gilbert Brown's place amongst his fellows. For a generation he has been a leader, indeed *the* leader of the anæsthetists of Australia.

Leadership is a quality which is not easily defined. Gilbert Brown does not possess it merely because he was the first President of the Australian Society of Anæsthetists, nor because he has received every distinction which organized anæsthesia in Australia can bestow. Leadership came to him because he was Gilbert Brown, a man well-equipped for the pioneering of anæsthesia in a young country. His achievement has been a threefold one, comprising organization, teaching and clinical research.

A generation ago Australia possessed some capable practitioners of anæsthesia, amongst whom were numbered Embley, Hornabrook, Green, Kasner Moss and Lidwill. There was, however, no organization of anæsthetists. Teaching scarcely existed other than by clinical apprenticeship. In 1929 the Third Session of the Australasian Medical Congress of the British Medical Association was held in Sydney. For the first time the Congress included a Section of Anæsthesia: its President was Gilbert Brown. The guest of honour was Francis

*Sources: Gilbert Brown's published papers are listed in the *Index Medicus* and the various journals of anæsthesia. Information as to his domestic life was kindly supplied by his son, Ian Brown, B.Sc. The record of his scientific activities exists amongst the papers of the Australian Society of Anæsthetists. For interpretations, of course, the writer takes sole personal responsibility.

Hoeffer McMechan of Cleveland, Ohio. This Congress marks the birth of organized anæsthesia in Australia. Brown and McMechan, more than any others, were its godparents.

In 1934 Gilbert Brown attended the Fourth Session of the Australasian Medical Congress in Hobart. A section of Anæsthesia was again included and, out of informal meetings of its members, the Australian Society of Anæsthetists was born. It is scarcely an over-statement to say that the Society came to birth in the lounge of Hadley's Hotel! Gilbert Brown was its first President. He guided it through its first General Meeting at Melbourne in 1935 and through the difficult years of its infancy. The position of the anæsthetist then, at least in Australia, was very different from the present one. Surgeons of the older school looked upon their anæsthetist as an unavoidable nuisance, as a mere technician whose highest virtue was prompt carrying-out of their own instructions. All too many of the anæsthetists were willing to accept this unflattering assessment of themselves. The early days of the Society were therefore difficult. Without Gilbert Brown's firm and tactful guidance, it might easily have encountered shipwreck. After holding the presidential office until 1939, Gilbert Brown continued to represent his State of South Australia upon the executive committee for a further seven years.

Gilbert—it is significant that his colleagues speak of him always by his Christian name—was already not without honour beyond the borders of Australia. In 1928 he was elected an Honorary Vice-President of the International Anæsthesia Research Society. In 1932 he was Vice-President *in absentia* of the Centenary Congress of the British Medical Association in London. In 1935 he made a study-tour of Great Britain and of Germany. The Diploma in Anæsthetics of the Conjoint Board in England was conferred upon him in 1936, and he became a Corresponding Fellow of the Association of Anæsthetists of Great Britain and Ireland. Neither was recognition lacking at home. He was repeatedly Chairman of the Section of Anæsthesia of the South Australian Branch of

GILBERT BROWN

the British Medical Association. In 1939 he was invited to deliver the triennial Embley Memorial Lecture in Melbourne, this being the highest compliment which the Victorian Branch of the British Medical Association can pay to an anæsthetist from another State.

In teaching, Gilbert has always taken a conspicuous place, many of the leading anæsthetists of Australia being his former pupils. For fourteen years he held the post of Instructor in Anæsthesia to the Medical and Dental Faculties of the University of Adelaide. He was, in fact, Lecturer in all but the name. When he retired in 1947, he saw to it that this title and its accompanying prestige were conferred upon his successor, although he had never troubled to ask them for himself. His teaching was always of a practical type. It was characterized by what Ralph Waters of Wisconsin terms " mule-sense ", a term coined to express the mental superiority of the mule to the proverbial horse. Gilbert Brown was one of the first medical teachers in Australia to make wide use of visual aids. His collection of lantern-slides is very large and is drawn, in the main, from his enormous series of personal administrations, to which further reference is made below.

Gilbert's contribution to clinical research has been material. In assessing it, however, the background of Australian medical practice must be taken into account. The country is not lacking in capable anæsthetists able to apply the discoveries of others in a duly critical way. It is, however, lacking in originators. The Australian anæsthetist gains his livelihood by private practice or by paid sessional work. Salaried appointments are of recent introduction and are still to be counted upon the fingers of the hands. Endowments for research in anæsthesia, whether in the Universities or the chemical industry, do not yet exist. In consequence the Australian anæsthetist can engage in research only as a spare-time occupation. A generation ago it was possible for an amateur of genius, such as Embley, to make important contributions to knowledge in this way. The problems of modern anæsthesia, however, are so complex that

they require the combined efforts of the pharmacologist, physiologist, anæsthetist and electrical or mechanical engineer. The research open to the Australian anæsthetist has therefore been, up to the present, of a clinical and observational type. It may be definitely valuable, but it is seldom original: the country can produce a Gilbert Brown, but not yet a Griffith or an Adriani.

It should be further noted that Gilbert Brown's professional life has been spent in the comparatively small city of Adelaide, in which the specialist practice of anæsthesia has only recently become economically possible. His modernity of outlook is all the more laudable for this fact. As each new agent or technique has entered anæsthesia, he has been amongst the first—and usually the very first—to employ it in South Australia. His published papers are many, as the attached bibliography shows. Their titles represent a veritable history of anæsthesia for the past forty years. Premedication, the endotracheal technique, nitrous oxide, intravenous anæsthesia, cyclopropane, "controlled respiration", curare, each innovation has appeared in turn and not very long after its introduction overseas. Together with this progressive outlook, Gilbert's papers show evidence of a sound knowledge of general medicine, of wide reading in his specialty and of an admirably judicial outlook. Their cardinal feature is intellectual honesty: Gilbert, a just but kindly critic of others, is unsparing in his criticism of himself. His experience is great. He cites, in a recent communication, 20,500 recorded administrations and this figure is far short of his total. He was the first anæsthetist in Australia to devote an individual record-sheet to each patient, and the first to follow McKesson in charting the blood pressure throughout operation. Perhaps his finest achievement in clinical reasearch is the Sub-Committee on Fatalities of the Royal Adelaide Hospital. For many years each fatality during anæsthesia in that Hospital has been made the subject of a systematic and candid inquiry. It is to be hoped that Gilbert Brown will use his newer leisure in arranging this material for publication, for it probably ranks with any such inquiry made anywhere in the world.

The life-story of a private person is rarely of interest to those unacquainted with him. In Gilbert Brown's case, however, the story is worth the telling. It will bring before the English reader some of the problems of medical pioneering in a young country. It will show also that the primary requirement of the pioneer is character. The present-day Australian has great admiration for his pioneer forefathers. As he surveys his prosperous little community, however, with its rapidly-expanding industrial potential, he is apt to think that the age of the pioneers ended a hundred years ago. This is not the case. In the arts and sciences, in medicine and aviation, in the production of atomic energy, Australia is still a " frontier " community in which the character and individualism of the pioneer can find scope.

Gilbert Brown was born in Wigan, Lancashire, in 1883. He can claim descent collaterally from Abbot Gilbert Brown of Sweetheart Abbey in Scotland, said to be the original of Scott's " Abbot ". His boyhood was spent in Ormskirk. To picture that environment, it is necessary to think of a grim and four-square house in a rather grim little town. In that house lived an old gentleman, also grim and four-square, who might have stepped out of a novel by Jane Austen: he was Gilbert's father. A boy brought up in that environment might be expected to possess the true Lancastrian tenacity of purpose, to be likewise taciturn and conservative. The key to much in Gilbert's later character is to be found in the setting and traditions of his early home.

After spending a year, at his father's wish, in the engineering course, Gilbert insisted upon a transfer to medicine. He was a good athlete and captained the Rugby football team of Liverpool University. He graduated M.B., Ch.B. in 1908 and held house appointments at the Royal Infirmary in Liverpool and at the Women's and Children's Hospitals. Even at that stage, he was interested in anæsthesia; his earliest paper, in the *Lancet* of 1911, dealt with pre-anæsthetic narcosis.

Gilbert was fortunate in having experience of travel during

his formative years. In 1905 he accompanied his brothers, who were engineers, on a journey into the less-known parts of Northern Canada. Later he visited the West Indies. In 1911 he travelled as ship's surgeon to Java, Hongkong, Japan and the Pacific Coast of America. He almost settled in Tacoma, Washington, and it is fortunate for the Australian Society of Anæsthetists that he did not.

Gilbert arrived in Australia in 1912 upon a reconnaissance which ended in permanent settlement. His motives for settling are obscure, but escape from the rigid environment of Ormskirk may well have been amongst them. He commenced general practice at Bute, and later at Snowtown, little communities situated about ninety miles north of Adelaide. Up-country practice in Australia still calls for the heroic virtues and must have called for an even greater share of them in 1912, before the aeroplane, the radio and the refrigerator had arrived to make the " Outback " tolerable. Gilbert, working as surgeon to three contiguous practices, did his rounds upon a motorcycle and later in a primitive Hupmobile car. The scenery has been described authoritatively as consisting of unlimited miles of red dust, magpies and barbed-wire fences.

Gilbert had proposed marriage, by letter, to Dr. Marie Simpson of London. She joined him in 1914, after a voyage which included being chased by the German commerce-raider *Emden*. Marrying on the day of her arrival in Adelaide, the Browns returned on the morrow to Snowtown. They had no money but abundance of resolution. The year was marked by a drought and a plague of mice. No one in the district could meet his bills and all were " carried " by the storekeepers. It is typical of Australian country people that, as soon as good seasons returned, almost all these debts were paid in full. It is amusing to picture Marie Brown, brought up amongst the London *intelligentsia*, precipitated into this world of dust, drought and financial stringency. Her domestic equipment consisted of a stout heart, a copy of Mrs. Beeton's cookery-book and a supply of " Glaxo ", which last had to take the

place of milk until the drought broke and there was once again feed for cows. Marie was not only the housewife; she was a partner in the practice and acted as Gilbert's anæsthetist.

During the First World War Gilbert's medical neighbours enlisted and left him with the care of all three practices. The authorities would not therefore sanction his own enlistment until 1918. In that year he went overseas as a captain in the Australian Army Medical Corps. He had got only to Durban when the Armistice was signed. On the homeward journey he did yeoman's service upon an influenza-stricken troopship. An even greater test of character occurred after his arrival in Australia, when he had to clean out a nest of inefficiency and corruption in a certain Quarantine Station.

In 1919 Gilbert embarked upon the venture of urban practice. He settled in Gilberton, a suburb of Adelaide, where he proved himself an excellent citizen and a pillar of the local Swimming Club, Men's Brotherhood and Masonic Lodge. His work at the Repatriation Hospital at Keswick, as anæsthetist to that wise surgeon Mr., later Sir, Henry Newland, marked the beginning of his serious interest in anæsthesia. From now on his story is synonymous with that of organized anæsthesia in Australia. It has been said that every surgeon should first serve an apprenticeship as an anæsthetist. It may be equally true that an anæsthetist should first serve an apprenticeship to surgery. Something of Gilbert's success in anæsthesia may well be due to his hard experience of rural surgery at Snowtown.

Adelaide being only a small metropolis, specialist anæsthesia has become possible only in the most recent times. Gilbert Brown was always obliged to combine his specialty with general practice, his wife acting as his partner. He was beyond the age of military service in the Second World War, but he did magnificent work upon the home front in his Hospitals and at the University. His wartime services to the Order of St. John of Jerusalem were recognised by the award of the insignia of a Serving Brother. In 1947 he retired from Hospital and University and has since devoted himself to private practice

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in anæsthesia. He has more leisure now than he has ever allowed himself in the past forty years. "Sometimes", he writes, "I blow into the Royal Adelaide and watch the lads for a time. I get more time in the medical library and have even been known to visit the Art Gallery". The social historian of the future may comment grimly on the fact that, domestic help being almost unknown in the Adelaide of 1948, Dr. Gilbert Brown is constrained to do many of his own domestic tasks!

It remains only to attempt a portrait. One needs to picture a tall, large-framed, rubicund man who still retains something of an athlete's leanness. His manner is slow, quiet and unobtrusive. He does not willingly assume leadership, partly because of temperamental barriers, partly because he can see both sides of any question and so finds action difficult. He is much in request as a chairman at meetings, since he believes in economy of words and knows when and how to exercise control over the proceedings. At scientific sessions he is characterized by a pipe and silence: it takes much to bring him to his feet, but what he then says is worth the saying. It is only when the discussion wanders from the rails that he will volunteer a statement, which is terse, pragmatic and relieved by dry and mordant humour. He has a trick of unexpected phraseology: general practice is to him "G.P-ery" and rash anæsthetic technique gives him "the in-squirms". He is a master of understatement: it is said that his comment, on first meeting his prospective daughter-in-law, was a laconic "She'll do!". He likes good wine and food and is an excellent host. Remembering his University days he retains a sympathetic interest in Rugby football. His amusements are "bad golf" and the reading of detective novels, which he calls "bloods". Beneath his carefully unemotional exterior is a wise, kindly and very experienced traveller along life's journey. For thirty years his knowledge, tact and *savoir-faire* have been at the disposal of the anæsthetists of Australia. He is the general father-confessor and a man who is much beloved.

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A STOMACH TUBE RETAINER

WITH the increasing popularity of curare and abdominal surgery, the use of a stomach tube should be a routine to ensure full control of stomach contents. Moreover the danger of inhalation of vomitus is thus avoided, even when an endo-bronchial tube, cuffed or otherwise, is not, for some reason, used. In addition, the inflation of the stomach during assisted respiration is avoided.

When a face mask is used with the stomach tube a sort of "grandfather's whiskers" problem arises as to the disposal of the stomach tube. If it is brought outside the mask and a reasonably gas-tight fit is to obtain between the the mask and the face, enough pressure will be exerted by the inflated brim of the face-piece to close the lumen of the tube. In such a case a sudden rush of stomach contents, as may occur in cases of intestinal obstruction, will flood up outside the tube and be inhaled into the bronchial tree. Placing the stomach tube inside the mask and depending on intermittent draining of stomach contents does little to solve the problem.

The only real safeguard is a steady unimpeded flow of the gastric contents well away from the laryngeal opening. The fitment illustrated solves these difficulties. It consists of an outer tubular case attached to a perforation in the mask (Fig. 1). Inside there is a cone-shaped attachment through which a channel is bored (Fig. 2). The fitment beds down in an air-tight seating, and is further secured by screwing firmly to the outer casing. The outlet is plugged by a cone metal cap on which is a small perforated bar on which to fit a Ryle's tube. The cap has an outlet bored to take a standard syringe nozzle to allow aspiration of the stomach contents. When not in use

an air-tight fitting is obtained by a small plug. A chain attached to the outer casing prevents loss of these parts.

When using a standard stomach tube it is pushed on to the cone and drains from the outlet when the cap is removed. The manufacturers have supplied an attachment to fit the outlet, which can be connected to any standard aspirator. When using a Ryle's tube it is threaded through the channel and fixed on to the cap where aspiration can take place.

The whole apparatus allows a complete gas-tight condition to obtain with or without the tubes attached, so that oxygen under pressure can be administered.

I am grateful for the expert advice of the directors of Willin Bros., New Cavendish Street, W.C., who made the apparatus for me.

A. Owen-Flood (London).

EVER-READY ADHESIVE TAPE

Adhesive strapping is in constant use by anæsthetists for a variety of purposes. Owing to the frailty of human nature, however, the roll of strapping has a way of disappearing from the anæsthetic trolley. When it is found and replaced, it cannot be used until the scissors, which have also disappeared, are likewise restored. The anæsthetist has then to stretch the desired length of strapping between his two hands, and wield the scissors with a third, while adjusting the apparatus with a fourth.

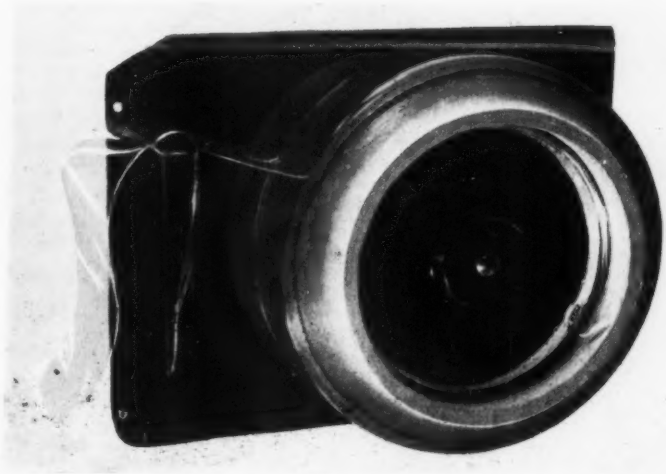
The device illustrated is designed for the anæsthetist with only two hands. It thwarts all but the most determined strapping purloiners and does away with the need for scissors.

It consists of a drum to carry a roll of Durex Cellulose tape (though other types of strapping can be used) and a serrated knife edge to cut it. The end of the tape is always free, and does not have to be dissected with the finger-nail. The desired length

FIG. 1

FIG. 2

A. O.-F.



Ever-Ready Adhesive Tape

R. W.

A method of reducing dead space

J. G. R.

is pulled off the roll and cut off on the knife edge with the finger and thumb of one hand.

The device is mounted beneath the top shelf or drawer of the anæsthetic trolley on one of the two front pillars, where it is accessible but does not encroach on needed space. It has been found convenient to have a pair—one being mounted on each side of the trolley and delivering quarter-inch and half-inch strapping respectively.

It is simple to make and can be produced by any competent mechanic.

RONALD WOOLMER (Bristol).

A METHOD OF REDUCING DEAD SPACE

THE inevitable increase in dead space, and in the resistance to respiration, which occur when a patient is made to respire from the orthodox continuous flow anæsthetic apparatus, render such apparatus unsuitable for use in small children. To overcome these difficulties I have been using for the past two years a circuit which is a modification of the Ayres T-piece adapted for use with a small facepiece. It consists of an angle-mount fitted to the facepiece and connected with a short length of wide-bore corrugated tubing. The angle-mount is pierced by a quarter-inch brass tube which leads into the facepiece and through which the fresh gases are fed to the patient. The stream of gases plays directly on to the face of the child and thus all dead space is eliminated, the corrugated tubing opens to the air so that all phases of respiration take place at atmospheric pressure.

J. G. REES (Liverpool).

NASO-TRACHEAL TUBES HELD UP AT THE CORDS: A REMEDY

Dr. J. G. Bourne (St. Thomas' Hospital) writes:

It sometimes happens that as the naso-tracheal tube is being introduced its tip sticks in the larynx above the vocal cords and cannot easily be made to pass through the glottis. This is more likely to occur if the tube is rather stiff and its curve marked.

If the situation is viewed with a laryngoscope, the tube will be seen to have run forward above the vocal cords and almost parallel to them, its tip being lodged just above their anterior commissure.

Getting the tip through the glottis may cause some delay and embarrassment. The glottis is V-shaped, with its point anterior and wide part posterior. If the tip of the tube can be displaced posteriorly it can usually be passed easily and gently through the cords. To do this Professor Macintosh, in his book *Essentials of General Anæsthesia*, suggests flexing the head acutely. In my hands this manœuvre is not always successful, and I have discovered a simpler, and, I think, more certain way of doing it.

My practice is to use a Macintosh laryngoscope to view the epiglottis until the tube has been seen to pass directly behind it and into the aditus of the larynx. The laryngoscope is then withdrawn, and with the right hand the tube is pressed gently onwards. If its tip is felt to be held up at the cords, the index finger of the left hand is placed across the throat at the level of the hyoid bone or thyreo-hyoid membrane. Firm backward pressure with this finger will now allow the tube to be passed quite easily into the trachea.

It need hardly be added that neither this nor any other method will succeed if the glottis is tightly closed in spasm.

REVIEWS

Modern Practice in Anæsthesia. Edited by FRANKIS T. EVANS. pp. 566. 227 illustrations. Butterworth's Medical Publications, London. Price 50*s*.

This is the third of the Modern Practice series to be published. It is indeed a handsome publication and a delight to have and to hold. The publishers are to be congratulated on the production of such a volume in these days of austerity.

The book consists of thirty-eight chapters written by twenty-four contributors, representative of the London school of anæsthesia. Because of the diversity of authorship it is inevitable to find great variety both in the style and quality of the writing. On the whole, terseness and clarity are lacking and their absence is not adequately compensated for by a plethora of gyratory diagrams which are not always themselves very clear.

The chapters are a mixed bag. Some of them are excellent, such as the fine chapter on the Preparation of the Patient, which should be read by all anæthetists, and that on Blood Transfusion and Fluid Replacement Therapy, which will serve to bring anæsthetists up to date with this most important facet of their work. It is useful to see clearly and concisely tabulated the types of patient who should not receive Rh positive blood.

Why must Dr. Morris inflict yet another stage of anæsthesia on us? Guedel originally described four stages of *ether* anæsthesia, and his classification has served anæsthetists well and has become universal. Disturbance of a standard classification is dangerous and to be justified must be supported by an appreciable weight of evidence to show that the old order was unsatisfactory. Dr. Morris does not supply this evidence. There is a lot to be said for the abolition of stages of anæsthesia, but there can be no support for this attempt to

complicate the position further. There is also a noticeable lack of appreciation that these stages do in fact relate only to ether and chloroform anæsthesia, and have been largely outmoded in modern techniques.

Spinal Anæsthesia is dealt with very adequately, as would be expected with this renowned editor, although one feels it is a pity that the techniques to which we have been introduced recently by Professor Hingson are not included. It is remarkable that so little emphasis is laid on the therapeutic implications of anæsthesia in this chapter and, in fact, throughout the book.

The section on Thoracic Anæsthesia is disappointing. As in other parts of the book, nowhere have we found a critical appraisal of the various techniques which are available. There is a surprising and notable lack of any real information on anæsthesia for children undergoing the operative treatment of congenital heart disease, nor is there any warning of the dangers inherent in patients with constrictive pericarditis. It would seem unnecessary to devote a full page coloured diagram to the normal circulation of the blood from the heart to the lungs and back (Plate 1); it would have been better to have coloured the more useful illustration of the effects of aerating one lung only (Figure 184).

It is debatable whether it is, as a policy, advisable to endeavour to compress into two chapters the whole of Physiology and Anatomy. The reviewer does not believe that there is such a thing as "Anatomy for the Anæsthetist" or that the Physiology of Anæsthesia is quite the same thing as Basic Physiology. Modern anæsthetists must have a very adequate knowledge of these subjects and these two chapters do not serve to impress the student of this necessity. It is surely inadequate to attempt an explanation of the "Composition, formation and functions of the Tissue Fluids" in a short paragraph of ten lines, or to dismiss the "Chemical transmission of Nerve Impulses" in eight lines, one of which contains a misprint which will give any reader food for thought (page 68, line 30).

There is no doubt that in this volume there is a wealth of information and it will certainly behove any candidate for the Diploma in Anæsthetics to peruse its pages, if only for the reason that he will see therein some of the teachings of his examiners. It is not a textbook; it is not intended to be. It is not a monograph. The question we must really decide is, does it, in fact, represent modern practice in anæsthesia? In the view of the reviewer it does not, for in such a treatise surely there can be no place for pictures and descriptions of out-moded pieces of apparatus such as that devised by Shipway, nor would one expect to find two and a half pages devoted to the open drop method of chloroform administration and a half-page illustration of the method of cutting " Bart's " chloroform lint. All this and no illustration of the omnipresent, much used and extremely efficient Boyle's Table, but presumably this was meant to be included, as the caption to an illustration of a Boyle's ether bottle reads, " Boyle's machine with Rotameters ".

This is a volume which will find its way into many countries overseas and will be taken to represent modern British practice. It is already too dated in its contents to be an adequate ambassador of the practice of British anæsthetists.

Medical Annual, 1949. Edited by Sir Henry Tidy and A. Rendle Short. pp. 44. 79 illustrations. 50 plates. John Wright & Sons Ltd., Bristol. 25*s*.

The Medical Annual, edited by Sir Henry Tidy and Dr. Rendle Short, is as usual a mine of useful information and it is difficult to find a better method of keeping up to date than the perusal year by year of its contents.

The reports of work done are by well known specialists and criticism of them would obviously be out of place unless the report itself were inaccurate, a very unlikely event. The source of original papers is to be found in the references and renders easy further study of any subject in which the reader is especially interested.

Dr. Langton Hewer, who writes the section on Analgesia and Anæsthesia, deals mostly with the accidents likely to occur in the course of the various methods reviewed.

Resuscitation and Anæsthesia for Wounded Men. By HENRY K. BEECHER, A.M., M.D. pp. xx and 161. 58 illustrations. Publisher: Charles C. Thomas, Springfield, Illinois. Price £2.

This is an excellent book, describing the observations of the author on men wounded during the Mediterranean campaign, 1943–45. It deals especially with the cause and management of traumatic shock. The author defines shock as " a disability of the circulatory system that parallels [is caused by] loss of effective blood volume and of hæmoglobin ". The whole book is devoted to an examination of this sentence.

The clinical aspects, both physiological and psychological, of shock are dealt with in the first section of the book and here the first correlation between severity of shock and blood loss is made. A good deal of space is rightly devoted to a consideration of the importance of clinical signs of shock and of the necessity for observing the direction of trends in blood pressure, pulse rate, and so on.

In the second section, the physiological derangements found in the recently wounded are described. It is perhaps in this section that most will be found which demands criticism, but only in matters of experimental detail; for instance, not all would agree that the method of estimating blood loss was strictly reliable. Nevertheless, the author establishes the correlation between blood volume and shock.

In the section on treatment of wounded men, the author shows himself to be a man of sound clinical judgement, who appreciates the importance of applied physiological principles to treatment. This is no more than would be expected from so distinguished an author.

In the final section on Anæsthesia, evidence is presented which shows, surprisingly enough, that ether is the anæsthetic of choice for use for the seriously wounded, and that next to this, Sodium Pentothal is the most valuable agent.

The book is profusely illustrated with photographs taken during the actions and includes a grim coloured sketch entitled "Shock Tent". Many of the histograms are rather difficult to understand at first sight. To have any merit, a diagram should present experimental findings in a manner which is obvious immediately. The reviewer feels that many of these diagrams could be missed out, since the information they contain is more clearly described in the accompanying text.

In fine, this book is to be recommended to all those interested in the problems arising out of traumatic shock as well as in the clinical applications of the knowledge gained by this careful work. It will also bring back clearly to those who were there the conditions which obtained at so many medical units in the field.

OBTUARY

THE news of the death of Dr. William-Lucien de Weerdt must have come as a very great shock to his many friends in this country. William de Weerdt received much of his training in anæsthesia in this country and had recently obtained the post of Lecturer in Anæsthesia at the University of Louvain. He was a keen and accomplished anæsthetist, and as a pioneer in his own country he had enormously enhanced the prestige of the specialty on the Continent. We would like to take this opportunity of offering to Madame de Weerdt the very deepest sympathy of his British colleagues.

Professor R. R. Macintosh writes:

" British anæsthetists will be grieved to hear of the death of their Belgian colleague Dr. W. de Weerdt. This gifted scholar had already written extensively on hæmatology and was marked out for distinction in general medicine when he turned his attention to anæsthetics. Sponsored by the British Council, and with strong letters of support from his University authorities, he commenced work in Oxford late in 1945. His academic background was quite out of the ordinary and he quickly grasped the essentials of safe anæsthesia. Unfortunately, because of his health, his stay in this country had to be cut short, but before returning to his own land he visited various other centres and founded friendships which were prized on both sides and which were cemented by regular correspondence."

ROYAL COLLEGE OF SURGEONS OF ENGLAND

FACULTY OF ANÆSTHETISTS

POSTGRADUATE LECTURES AND TUTORIALS IN ANÆSTHETICS

Spring, 1950

Lectures

A course of 45 Lectures in Anæsthesia will be given at the College from 12th April to 2nd May, 1950. It is proposed to give three lectures daily (at 12 noon, 3-45 p.m. and 5-0 p.m.) from Monday to Friday for a period of three consecutive weeks.

The fee for the whole course is £15 15s. od., Fellows and Members of the College and Members of the Faculty of Anæsthetists will be admitted on payment of a fee of £12 12s. od.

The complete list of Lecturers and their subjects may be obtained upon application.

Tutorials

A series of Tutorials in Anæsthetics will be held during the same period as the Lectures, and will consist of ten one-hourly periods, commencing at 6-15 p.m. These are only open to those who are also attending the Lecture course.

Basic Sciences

A course of 72 Lectures in Anatomy, Applied Physiology, and Pathology is being held in the College from April to June 1950. A special course of 10 Pharmacology Lectures will be held from 27th March to 31st March, 1950, at 5-0 p.m. and 6-15 p.m. each evening.

A limited amount of residential accommodation is available in the College for students attending courses. Full details may be obtained on application. Lunch, tea and dinner are obtainable in the College daily.

Applications, accompanied by a cheque for the appropriate fee, should be sent to the Secretary, Faculty of Anæsthetists, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2.

H. EDMUND G. BOYLE